



# REsearch UPDATES

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**IN THIS ISSUE:** Cancer prevention is complex, and when considering it, one must take into account many different things. Druesne-Pecollo et al. found that beta carotene supplements are not recommended for cancer prevention, but Chaiter et al. found that dietary carotenoids can help prevent colorectal cancer. However, this benefit can be cancelled or reversed by smoking. Hermann and others also connected smoking, alcohol consumption, and colorectal cancer. Toriola and associates found a connection between alcohol consumption and cancer in men. For women, physical activity in adulthood was protective against developing endometrial cancer according to John and associates, and in our study of the month, Brasky and colleagues found that fish oil supplements can protect against breast cancer. So it's important to look at the whole picture when it comes to cancer prevention, because some things in isolation of each other do not necessarily produce the benefits produced by putting them all together.

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## BREAST CANCER



De Silva, M, U. Senarath, M. Gunatilake et al.

### **Prolonged Breastfeeding Reduces Risk of Breast Cancer in Sri Lankan Women: A Case-Control Study.**

*Cancer Epidemiology.* 2010 June; 343: 267-273.

**GOAL:** To assess the association between duration of breastfeeding and the risk of breast cancer in Sri Lankan women. **METHODS:** We conducted a case-control study in women aged 30-64 years in selected health care facilities in the Western province. A total of 100 recent cases of breast cancer (histologically confirmed) and 203 controls (age and parity matched) were included. Detailed information regarding breastfeeding, menstruation, reproductive factors, passive smoking and other confounders was collected using a structured questionnaire. Adjusted odds ratios and 95% confidence intervals were calculated using multiple logistic regressions.

**PRINCIPAL RESULTS:** Multivariate analysis found that those women who breastfed for [greater-than or equal to] 24 months during lifetime had significantly lower risk of breast cancer than those who breastfed for less than 24 months (OR = 0.40; 95%CI = 0.22, 0.73). Compared to 0-11 months of lifetime breastfeeding, there was a 66.3% reduction in breast cancer risk in women who breastfed for 12-23 months, 87.4% reduction in 24-35 months and 94% reduction in 36-47 months categories. The mean duration of breastfeeding per child for [greater-than or equal to] 12 months was also associated with reduced risk of breast cancer (OR = 0.52; 95%CI = 0.28, 0.94). The significant factors associated with increased risk of breast cancer were: post-menopausal women (OR = 1.74; 95%CI = 1.01, 3.01); having an abortion in the past (OR = 3.42; 95%CI = 1.75, 6.66) and exposure to passive smoking (OR = 2.96, 95%CI = 1.53, 5.75).

**MAJOR CONCLUSIONS:** Prolonged breastfeeding significantly reduces the risk of breast cancer and this protective effect was supported by a dose-response relationship. Risk due to passive smoking should be emphasized in anti-smoking programmes.



## BETA CAROTENE

Druesne-Pecollo, N, P. Latino-Martel, T. Norat, et al.

### Beta-Carotene Supplementation and Cancer Risk: A Systematic Review and Metaanalysis of Randomized Controlled Trials

*International Journal of Cancer.* 2010 Jul 1; 1271: 172-184.

**BACKGROUND:** The effect of beta-carotene supplementation on cancer incidence has been investigated in several randomized controlled trials. **OBJECTIVE:** The objective was to review the effect of beta-carotene supplementation on cancer incidence in randomized trials by cancer site, beta-carotene supplementation characteristics and study population. **METHODS:** Relevant trials were retrieved by searching PubMed (up to April 2009). Authors involved in selected studies were contacted for additional information. Thirteen publications reporting results from 9 randomized controlled trials were included.

**RESULTS:** Overall, no effect of beta-carotene supplementation was observed on the incidence of all cancers combined (RR, 1.01; 95% CI, 0.98-1.04), pancreatic cancer (RR, 0.99; 95% CI, 0.73-1.36), colorectal cancer (RR, 0.96; 95% CI, 0.85-1.09), prostate cancer (RR, 0.99; 95% CI, 0.91-1.07), breast cancer (RR, 0.96; 95% CI, 0.85-1.10), melanoma (RR, 0.98; 95% CI, 0.65-1.46) and non melanoma skin cancer (RR, 0.99; 95% CI, 0.93-1.05). The incidence of lung and stomach cancers were significantly increased in individuals supplemented with beta-carotene at 20-30 mg day<sup>-1</sup> (RR, 1.16; 95% CI, 1.06-1.27 and RR, 1.34; 95% CI, 1.06-1.70), in smokers and asbestos workers (RR, 1.20; 95% CI, 1.07-1.34 and RR, 1.54; 95% CI, 1.08-2.19) compared to the placebo group. Beta-carotene supplementation has not been shown to have any beneficial effect on cancer prevention. Conversely, it was associated with increased risk not only of lung cancer but also of gastric cancer at doses of 20-30 mg day<sup>-1</sup>, in smokers and asbestos workers.

**CONCLUSION:** This study adds to the evidence that nutritional prevention of cancer through beta-carotene supplementation should not be recommended.

## LUNG CANCER

Johansson M, Relton C, Ueland PM, et al.

### Serum B Vitamin Levels and Risk of Lung Cancer.

*J Am Med Assoc.* 2010 Jun 16; 23303: 2377.

**CONTEXT:** B vitamins and factors related to 1-carbon metabolism help to maintain DNA integrity and regulate gene expression and may affect cancer risk. **OBJECTIVE:** To investigate if 1-carbon metabolism factors are associated with onset of lung cancer. **DESIGN, SETTING, AND PARTICIPANTS:** The European Prospective Investigation into Cancer and Nutrition (EPIC) recruited 519,978 participants from 10 countries between 1992 and 2000, of whom 385,747 donated blood. By 2006, 899 lung cancer cases were identified and 1770 control participants were individually matched by country, sex, date of birth, and date of blood collection. Serum levels were measured for 6 factors of 1-carbon metabolism and cotinine. **MAIN OUTCOME MEASURE:** Odds ratios (ORs) of lung cancer by serum levels of 4 B vitamins (B(2), B(6), folate [B(9)], and B(12)), methionine, and homocysteine.

**RESULTS:** Within the entire EPIC cohort, the age-standardized incidence rates of lung cancer (standardized to the world population, aged 35-79 years) were 6.6, 44.9, and 156.1 per 100,000 person-years among never, former, and current smokers for men, respectively. The corresponding incidence rates for women were 7.1, 23.9, and 100.9 per 100,000 person-years, respectively. After accounting for smoking, a lower risk for lung cancer was seen for elevated serum levels of B(6) (fourth vs. first quartile OR, 0.44; 95% confidence interval [CI], 0.33-0.60; P for trend <.000001), as well as for serum methionine (fourth vs. first quartile OR, 0.52; 95% CI, 0.39-0.69; P for trend <.000001). Similar and consistent decreases in risk were observed in never, former, and current smokers, indicating that results were not due to confounding by smoking. The magnitude of risk was also constant with increasing length of follow-up, indicating that the associations were not

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explained by preclinical disease. A lower risk was also seen for serum folate (fourth vs. first quartile OR, 0.68; 95% CI, 0.51-0.90; P for trend = .001), although this was apparent only for former and current smokers. When participants were classified by median levels of serum methionine and B(6), having above-median levels of both was associated with a lower lung cancer risk overall (OR, 0.41; 95% CI, 0.31-0.54), as well as separately among never (OR, 0.36; 95% CI, 0.18-0.72), former (OR, 0.51; 95% CI, 0.34-0.76), and current smokers (OR, 0.42; 95% CI, 0.27-0.65).

**CONCLUSION:** Serum levels of vitamin B(6) and methionine were inversely associated with risk of lung cancer.

## ENDOMETRIAL CANCER

John, EM, J. Koo and P. L. Horn-Ross.

### Lifetime Physical Activity and Risk of Endometrial Cancer.

*Cancer Epidemiology Biomarkers and Prevention.* 2010 May; 195: 1276-1283.

**BACKGROUND:** The role of moderate physical activity and life patterns of activity in reducing endometrial cancer risk remains uncertain. **METHODS:** We assessed lifetime histories of activity from recreation, transportation, chores, and occupation and other risk factors in a population-based case-control study of endometrial cancer conducted in the San Francisco Bay area. The analysis was based on 472 newly diagnosed cases ascertained by the regional cancer registry and 443 controls identified by random-digit dialing who completed an in-person interview.

**RESULTS:** Reduced risks associated with greater lifetime physical activity (highest versus lowest tertile) were found for both total activity [odds ratio (OR), 0.61; 95% confidence interval (95% CI), 0.43-0.87; P trend = 0.01] and activity of moderate intensity (OR, 0.44; 95% CI, 0.30-0.64; P trend < 0.0001). Compared with women with low lifetime physical activity (below median), those with greater activity throughout life had a higher reduction in risk (OR, 0.62; 95% CI, 0.44-0.88). Inverse associations were stronger in obese and overweight women, but differences were not statistically significantly different from those in normal-weight women.

**CONCLUSION:** These findings suggest that physical activity in adulthood, even of moderate intensity, may be effective in lowering the risk of endometrial cancer, particularly among those at highest risk for this disease. **IMPACT:** The results emphasize the importance of evaluating lifetime histories of physical activity from multiple sources, including both recreational and non-recreational activities of various intensities, to fully understand the relation between physical activity and disease risk.

## GASTRIC CANCER

Ko, K-, S. K. Park, B. Park, et al.

### Isoflavones from Phytoestrogens and Gastric Cancer Risk: A Nested Case-Control Study within the Korean Multicenter Cancer Cohort.

*Cancer Epidemiology Biomarkers and Prevention.* 2010 May; 195: 1292-1300.

**BACKGROUND:** The role of soybean products in gastric cancer risk is not clear in epidemiologic studies due to measurement error from dietary intake questionnaires and due to different degrees of bias according to study design. To examine the association between soybean products and gastric cancer risk, we measured phytoestrogen biological markers in a nested case-control study. **METHODS:** The study population was composed of 131 cases and 393 matched controls within the Korean Multicenter Cancer Cohort. The concentrations of the four biomarkers in the plasma samples were measured using time-resolved fluoroimmunoassay. Conditional and unconditional logistic regression models were used to compute the odds ratio (OR) and 95% confidence intervals (CI).

**RESULTS:** Median plasma concentrations of genistein (229 nmol/L for controls, 181.8 nmol/L for cases; P = 0.07) and daidzein (131.2 nmol/L for controls, 80.5 nmol/L for cases; P = 0.04) in cases were lower than in controls, whereas equal concentrations were similar. Compared with the reference group, gastric cancer risk decreased in the highest groups for genistein (OR, 0.54; 95% CI, 0.31-0.93) and daidzein (OR, 0.21; 95% CI,



0.08-0.58). Higher equal concentrations were associated with a decreased risk for gastric cancer (OR, 0.50; 95% CI, 0.27-0.90). The combination of the highest concentrations for each isoflavone category was associated with a 0.09-fold decreased risk for gastric cancer compared with the combination of the lowest concentrations for each category. There was no association between plasma lignan concentrations and gastric cancer.

**CONCLUSIONS:** High serum concentrations of isoflavones were associated with a decreased risk for gastric cancer. **IMPACT:** These results suggest a beneficial effect of high soybean product intake for gastric cancer risk.

## PANCREATIC CANCER

Polesel, J, R. Talamini, E. Negri, et al.

### Dietary Habits and Risk of Pancreatic Cancer: An Italian Case-Control Study.

*Cancer Causes and Control.* 2010 April; 214: 493-500.

**OBJECTIVE:** To investigate the association between dietary habits and pancreatic cancer. **METHODS:** Between 1991 and 2008, we conducted a hospital-based case-control study in northern Italy. **CASES:** 326 patients (median age 63 years) with incident pancreatic cancer admitted to general hospitals in the areas of Milan and Pordenone, northern Italy. **CONTROLS:** 652 patients (median age 63 years) with acute non-neoplastic conditions admitted to the same hospital network of cases. Diet was assessed using a validated food frequency questionnaire. Conditional logistic regression was used to estimate odds ratios (OR) and the corresponding 95% confidence intervals (CI).

**RESULTS:** Frequent meat consumption was associated to a twofold increased risk of pancreatic cancer (95% CI: 1.18-3.36); the risk was significant for meat cooked by boiling/ stewing or broiling/roasting. Added table sugar (OR = 2.23; 95% CI: 1.34-3.71) and potatoes (OR = 1.79; 95% CI: 1.12-2.86) were related to pancreatic cancer. An inverse association emerged for non-citrus fruits (OR = 0.41; 95% CI: 0.24-0.69), cooked vegetables (OR = 0.57; 95% CI: 0.36-0.92), and, possibly, for pulses (OR = 0.59; 95% CI: 0.35-1.00).

**CONCLUSIONS:** The present study supports an inverse association between fruits and vegetables and pancreatic cancer risk, and it confirms a direct relation with meat. The increased risk for table sugar suggests that insulin resistance may play a role in pancreatic carcinogenesis.

## COLORECTAL CANCER

Chaiter, Y, S. B. Gruber, A. Ben-Amotz, et al.

### Smoking Attenuates the Negative Association between Carotenoids Consumption and Colorectal Cancer Risk.

*Cancer Causes & Control.* 2009 Oct; 208: 1327-1338.

**OBJECTIVES:** Consumption of vegetables and fruits, physical activity, obesity and caloric intake are all strongly related to the risk of colorectal cancer (CRC). The association between dietary intake of carotenoids from vegetables/fruits and risk of CRC in the context of cigarette smoking was studied in a nutritionally diverse population. **METHODS:** The study included 1,817 age sex residence-matched case-control pairs from a population-based study in Northern Israel. Data were acquired by food-frequency questionnaire. Individual intake of carotenoid isomers was calculated using an Israeli food content database. Odds ratios (ORs) were calculated using conditional logistic regression models adjusted for known risk factors.

**RESULTS:** Strong inverse associations were found with consumption of 9-cis-beta-carotene (OR = 0.35, 0.26-0.47), all-trans-beta-carotene (OR = 0.58, 0.44-0.76), cis-beta-cryptoxanthin (OR = 0.67, 0.50-0.90), all-trans-zeaxanthin (OR = 0.64, 0.48-0.86), and lutein (OR = 0.74, 0.57-0.96). Lycopene (OR = 2.22, 1.71-2.89) and all-trans-beta-cryptoxanthin (OR = 2.01, 1.48-2.73) were associated with increased risk of CRC. Inverse associations of most carotenoids with CRC, demonstrated in non-smokers, were much attenuated or reversed in past or current smokers with a highly significant interaction term.

**CONCLUSIONS:** Consumption of most dietary carotenoids was found to be strongly associated with reduced risk of CRC. However, smoking significantly attenuated or reversed this observed protective effect



on CRC occurrence. Smokers should be advised that smoking also hampers the potential health promoting effects of high fruit and vegetable consumption.

Hermann, S, S. Rohrmann and J. Linseisen.

### **Lifestyle Factors, Obesity and the Risk of Colorectal Adenomas in EPIC-Heidelberg.**

*Cancer causes & control* : CCC. 2009 Oct; 208: 1397-1408.

**OBJECTIVE:** We investigated the association of lifestyle and obesity with colorectal adenoma risk in a prospective setting. **METHODS:** At recruitment (1994-1998), information on diet, anthropometry, lifestyle, and medication was assessed in 25,540 participants of the EPIC-Heidelberg cohort. Until June 2007, 536 verified incident colorectal adenomas were identified. Furthermore, participants with negative colonoscopy (n = 3966) were included in the analytic cohort.

**RESULTS:** In multivariate logistic regression analyses, participants with highest alcohol intake had an increased adenoma risk (odds ratio [OR] = 1.63; 95% CI 1.21-2.22) compared with lowest intake group. Folate consumption modified the ethanol effect (p-interaction = 0.03). Current smokers had a significantly increased adenoma risk compared with never smokers (OR = 1.40; 95% CI 1.16-1.84). Regular NSAID intake was associated with lower risk in subjects who reported their use at least twice compared with nonusers (OR = 0.70; 95% CI 0.53-0.93). Physical activity, body mass index, and waist-to-hip ratio were not consistently associated with adenoma risk.

**CONCLUSIONS:** The results of this prospective cohort study showed that alcohol intake and smoking are important risk factors for colorectal adenoma, and regular NSAID use decreases the risk. The relationship between alcohol consumption and adenoma risk was modified by folate intake. However, we could not confirm an effect of obesity or physical activity on adenoma risk.

## ALCOHOL CONSUMPTION

Toriola, AT, S. Kurl, T. Dyba, et al.

### **The Impact of Alcohol Consumption on the Risk of Cancer among Men: A 20-Year Follow-Up Study from Finland.**

*Eur J Cancer*. 2010 June; 469: 1488-1492.

**INTRODUCTION:** Alcohol consumption is associated with certain cancer types and cancer deaths but there is paucity of information on the relationship between alcohol and total cancer risk. Hence, we examined this association. **METHODS:** We analysed data from a prospective population-based cohort study of 2627 men from Eastern Finland who had no history of cancer at baseline. There were 515 incident cancer cases accrued over 52,540 person years during the 20 years of follow-up.

**RESULTS:** We observed a linear relationship between alcohol consumption and cancer. Men within the highest quintile of alcohol consumption (>115 g/week) had a 42% increased risk of total cancer compared with those within the lowest quintile (relative risk (RR) 1.42, 95% confidence interval (CI) 1.07-1.88; P-trend = 0.03) after adjusting for age, smoking, total energy intake and cardio-respiratory fitness. The results were the same after excluding cancer cases diagnosed during the first 2 years of follow-up. Men who consumed [greater-than or equal to] 28.2 g/day of alcohol (median) had a relative risk of 1.22, 95% CI 1.03-1.46; P-value 0.03) compared to those who consumed less.

**CONCLUSION:** About 6.7% of the cancer cases in this cohort were due to alcohol consumption. Strategies to reduce cancer burden need to incorporate reduction in alcohol consumption, probably beyond the level currently recommended.



## STUDY OF THE MONTH

Brasky TM, Lampe JW, Potter JD, Patterson RE, White E.

### Specialty Supplements and Breast Cancer Risk in the VITamins And Lifestyle (VITAL) Cohort.

*Cancer Epidemiol Biomarkers Prev.* 2010 197: 1696-708.

**BACKGROUND:** Use of nonvitamin, nonmineral "specialty" supplements has increased substantially over recent decades. Several supplements may have anti-inflammatory or anticancer properties. Additionally, supplements taken for symptoms of menopause have been associated with reduced risk of breast cancer in two case-control studies. However, there have been no prospective studies of the association between the long-term use of these supplements and breast cancer risk. **METHODS:** Participants were female members of the VITamins And Lifestyle (VITAL) Cohort. Postmenopausal women, ages 50 to 76 years, who were residents of western Washington State, completed a 24-page baseline questionnaire in 2000 to 2002 (n = 35,016). Participants were queried on their recency (current versus past), frequency (days/week), and duration (years) of specialty supplement use. Incident invasive breast cancers (n = 880) from 2000 to 2007 were obtained from the Surveillance, Epidemiology, and End Results registry. Multivariable-adjusted hazards ratios (HR) and 95% confidence intervals (95% CI) were estimated by Cox proportional hazards models.

**RESULTS:** Current use of fish oil was associated with reduced risk of breast cancer (HR, 0.68; 95% CI, 0.50-0.92). Ten-year average use was suggestive of reduced risk (P trend = 0.09). These results held for ductal but not lobular cancers. The remaining specialty supplements were not associated with breast cancer risk: Specifically, use of supplements sometimes taken for menopausal symptoms (black cohosh, dong quai, soy, or St. John's wort) was not associated with risk.

**CONCLUSIONS:** Fish oil may be inversely associated with breast cancer risk. **IMPACT:** Fish oil is a potential candidate for chemoprevention studies. Until that time, it is not recommended for individual use for breast cancer prevention.

## ELECTRONIC RESEARCH UPDATES - BONUS ABSTRACTS

### BREAST CANCER

Bradshaw, PT, S. K. Sagiv, G. C. Kabat, et al.

### Consumption of Sweet Foods and Breast Cancer Risk: A Case-Control Study of Women on Long Island, New York.

*Cancer causes & control : CCC.* 2009 Oct; 208: 1509-1515.

**BACKGROUND:** Several epidemiologic studies have reported a positive association between breast cancer risk and high intake of sweets, which may be due to an insulin-related mechanism. **METHODS:** We investigated this association in a population-based case-control study of 1,434 cases and 1,440 controls from Long Island, NY. Shortly after diagnosis, subjects were interviewed in-person to assess potential breast cancer risk factors, and self-completed a modified Block food frequency questionnaire, which included 11 items pertaining to consumption of sweets (sweet beverages, added sugars, and various desserts) in the previous year. Using unconditional logistic regression models, we estimated the association between consumption of sweets and breast cancer.

**RESULTS:** Consumption of a food grouping that included dessert foods, sweet beverages, and added sugars was positively associated with breast cancer risk [adjusted odds ratio (OR) comparing the highest to the lowest quartile: 1.27, 95% confidence interval (CI): 1.00-1.61]. The OR was slightly higher when only dessert foods were considered (OR: 1.55, 95% CI: 1.23-1.96). The association with desserts was stronger among pre-menopausal women (OR: 2.00, 95% CI: 1.32-3.04) than post-menopausal women (OR: 1.40, 95% CI: 1.07-1.83), although the interaction with menopause was not statistically significant.

**CONCLUSION:** Our study indicates that frequent consumption of sweets, particularly desserts, may be associated with an increased risk of breast cancer. These results are consistent with other studies that implicate insulin-related factors in breast carcinogenesis.



## PANCREATIC CANCER

Bao, Y, K. Ng, B. M. Wolpin, et al.

### Predicted Vitamin D Status and Pancreatic Cancer Risk in Two Prospective Cohort Studies.

*Br J Cancer.* 2010 April; 1029: 1422-1427.

**BACKGROUND:** Studies evaluating vitamin D status in relation to pancreatic cancer risk have yielded inconsistent results. **METHODS:** We prospectively followed 118 597 participants in the Nurses' Health Study and Health Professionals Follow-up Study from 1986 to 2006. We calculated a 25-hydroxyvitamin D (25(OH)D) score from known predictors of vitamin D status for each individual and then examined the predicted 25(OH)D levels in relation to pancreatic cancer risk. Relative risks (RRs) and 95% confidence intervals (95% CIs) were estimated using Cox proportional hazards models adjusted for age, sex, race, height, smoking, and diabetes. We then further adjusted for body mass index (BMI) and physical activity in a sensitivity analysis.

**RESULTS:** During 20 years of follow-up, we identified 575 incident pancreatic cancer cases. Higher 25(OH)D score was associated with a significant reduction in pancreatic cancer risk; compared with the lowest quintile, participants in the highest quintile of 25(OH)D score had an adjusted RR of 0.65 (95% CI 0.50-0.86; P trend 0.001). Results were similar when we further adjusted for BMI and physical activity.

**CONCLUSIONS:** Higher 25(OH)D score was associated with a lower risk of pancreatic cancer in these two prospective cohort studies.

Gong, Z, E. A. Holly and P. M. Bracci.

### Intake of Folate, Vitamins B6, B12 and Methionine and Risk of Pancreatic Cancer in a Large Population-Based Case-Control Study.

*Cancer causes & control : CCC.* 2009 Oct; 208: 1317-1325.

**OBJECTIVE:** Folate and other methyl-group nutrients may play a key role in pancreatic carcinogenesis through their effects on DNA integrity. We examined the association between pancreatic cancer and intake of folate, vitamins B(6), B(12) and methionine in a large population-based case-control study. **METHODS:** Risk factor data were collected during in-person interviews with 532 pancreatic cancer cases diagnosed in 1995-1999 and 1,701 frequency-matched controls in the San Francisco Bay Area. Dietary history and supplement use were obtained using a semi-quantitative food-frequency questionnaire developed at Harvard University. Adjusted unconditional logistic regression was used to compute odds ratios (OR) and 95% confidence intervals (CI) as estimates of the relative risk.

**RESULTS:** Total folate intake was inversely associated with pancreatic cancer (5th vs. 1st quintile: OR = 0.67, 95% CI = 0.48-0.93, p (trend) = 0.04). Increased vitamin B(12) from food was positively associated with pancreatic cancer although risk estimates for quintiles 3-5 were similar (5th vs. 1st quintile: OR = 1.9, 95% CI = 1.3-2.6, p (trend) = 0.001). Intake of vitamin B(6) or methionine was not associated with pancreatic cancer risk.

**CONCLUSIONS:** Our study provided some support for an inverse association between folate intake and pancreatic cancer risk. The increased pancreatic cancer risk with vitamin B(12) intake from food warrants further investigation.

## COLORECTAL CANCER

Miller, PE, P. Lazarus, S. M. Lesko, et al.

### Diet Index-Based and Empirically Derived Dietary Patterns are Associated with Colorectal Cancer Risk.

*J Nutr.* 2010 July; 1407: 1267-1273.

**BACKGROUND:** Previous studies have derived patterns by measuring compliance with pre-established dietary guidance or empirical methods, such as principal components analysis (PCA). **OBJECTIVE:** Our



objective was to examine colorectal cancer risk associated with patterns identified by both methods. **METHODS:** The study included 431 incident colorectal cancer cases (225 men, 206 women) and 726 healthy controls (330 men, 396 women) participating in a population-based, case-control study. PCA identified sex-specific dietary patterns and the Healthy Eating Index-2005 (HEI-05) assessed adherence to the 2005 Dietary Guidelines for Americans. A fruits and vegetables pattern and a meat, potatoes, and refined grains pattern were identified among men and women; a third pattern (alcohol and sweetened beverages) was identified in men.

**RESULTS:** The fruits and vegetables pattern was inversely associated with risk among men [odds ratio (OR) = 0.38, 95% CI = 0.21-0.69 for the highest compared with the lowest quartile] and women (OR = 0.35, 95% CI = 0.19-0.65). The meat, potatoes, and refined grains pattern was positively associated with risk in women (OR = 2.20, 95% CI = 1.08-4.50) and there was a suggestion of a positive association among men (OR = 1.56, 95% CI = 0.84-2.90; P-trend = 0.070). Men and women with greater HEI-05 scores had a significantly reduced risk of colorectal cancer (OR = 0.56, 95% CI = 0.31-0.99; OR = 0.44, 95% CI = 0.24-0.77, respectively).

**CONCLUSION:** Following the Dietary Guidelines or a dietary pattern lower in meat, potatoes, high fat, and refined foods and higher in fruits and vegetables may reduce colorectal cancer risk.

## PROSTATE CANCER

Collin, SM, C. Metcalfe, H. Refsum, et al.

### Circulating Folate, Vitamin B12, Homocysteine, Vitamin B 12 Transport Proteins, and Risk of Prostate Cancer: A Case-Control Study, Systematic Review, and Meta-Analysis.

*Cancer Epidemiology Biomarkers and Prevention.* 2010 June; 196: 1632-1642.

**BACKGROUND:** Disturbed folate metabolism is associated with an increased risk of some cancers. Our objective was to determine whether blood levels of folate, vitamin B12, and related metabolites were associated with prostate cancer risk. **METHODS:** Matched case-control study nested within the U.K. population-based Prostate testing for cancer and Treatment ( ProtecT) study of prostate-specific antigen - detected prostate cancer in men ages 50 to 69 years. Plasma concentrations of folate, B12 (cobalamin), holo-haptocorrin, holo-transcobalamin total transcobalamin, and total homocysteine (tHcy) were measured in 1,461 cases and 1,507 controls. ProtecT study estimates for associations of folate, B12, and tHcy with prostate cancer risk were included in a meta-analysis, based on a systematic review.

**RESULTS:** In the ProtecT study, increased B12 and holo-haptocorrin concentrations showed positive associations with prostate cancer risk [highest versus lowest quartile of B12 odds ratio (OR) = 1.17 (95% confidence interval, 0.95-1.43); P-trend = 0.06; highest versus lowest quartile of holo-haptocorrin OR = 1.27 (1.04-1.56); P-trend = 0.01]; folate, holo-transcobalamin, and tHcy were not associated with prostate cancer risk. In the meta-analysis, circulating B12 levels were associated with an increased prostate cancer risk [pooled OR = 1.10 (1.01-1.19) per 100 pmol/L increase in B12; P = 0.002]; the pooled OR for the association of folate with prostate cancer was positive [OR = 1.11 (0.96-1.28) per 10 nmol/L; P = 0.2] and conventionally statistically significant if ProtecT (the only case-control study) was excluded [OR = 1.18 (1.00-1.40) per 10 nmol/L; P = 0.02].

**CONCLUSION:** Vitamin B12 and (in cohort studies) folate were associated with increased prostate cancer risk. **IMPACT:** Given current controversies over mandatory fortification, further research is needed to determine whether these are causal associations.





## SKIN CANCER

Dennis, LK, C. F. Lynch, D. P. Sandler et al.

### **Pesticide use and Cutaneous Melanoma in Pesticide Applicators in the Agricultural Health Study.**

*Environ Health Perspect.* 2010 June; 1186: 812-817.

**BACKGROUND:** Melanoma rates continue to increase; however, few risk factors other than sun sensitivity and ultraviolet radiation (including sun exposure) have been identified. Although studies of farmers have shown an excess risk of melanoma and other skin cancers, it is unclear how much of this is related to sun exposure compared with other agricultural exposures. **METHODS:** We examined dose-response relationships for 50 agricultural pesticides and cutaneous melanoma incidence in the Agricultural Health Study cohort of licensed pesticide applicators, along with ever use of older pesticides that contain arsenic. Logistic regression was used to examine odds ratios (ORs) and 95% confidence intervals (CIs) associated with pesticide exposure adjusted for age, sex, and other potential confounders.

**RESULTS:** We found significant associations between cutaneous melanoma and maneb/mancozeb ([greater-than or equal to] 63 exposure days: OR = 2.4; 95% CI, 1.2-4.9; trend  $p = 0.006$ ), parathion ([greater-than or equal to] 56 exposure days: OR = 2.4; 95% CI, 1.3-4.4; trend  $p = 0.003$ ), and carbaryl ([greater-than or equal to] 56 exposure days: OR = 1.7; 95% CI, 1.1-2.5; trend  $p = 0.013$ ). Other associations with benomyl and ever use of arsenical pesticides were also suggested.

**CONCLUSIONS:** Most previous melanoma literature has focused on host factors and sun exposure. Our research shows an association between several pesticides and melanoma, providing support for the hypotheses that agricultural chemicals may be another important source of melanoma risk.

## RENAL CELL CARCINOMA

Hu, J, C. La Vecchia, E. Negri, et al.

### **Dietary Vitamin C, E, and Carotenoid Intake and Risk of Renal Cell Carcinoma.**

*Cancer causes & control : CCC.* 2009 Oct; 208: 1451-1458.

**OBJECT:** The study examines the association between dietary intake of vitamin C, E, and carotenoids and the risk of renal cell carcinoma (RCC). **METHODS:** Between 1994 and 1997 in 8 Canadian provinces, mailed questionnaires were completed by 1,138 incident, histologically confirmed cases of RCC and 5,039 population controls, including information on socio-economic status, lifestyle habits and diet. A 69-item food frequency questionnaire provided data on eating habits 2 years before data collection. Odds ratios (OR) and 95% confidence intervals (CI) were computed using unconditional logistic regression.

**RESULTS:** Dietary intake of beta-carotene and lutein/zeaxanthin was inversely associated with the risk of RCC. The ORs for the highest versus the lowest quartile were 0.74 (95% CI, 0.59-0.92) and 0.77 (95% CI, 0.62-0.95), respectively. The significant inverse association with beta-carotene and lutein/zeaxanthin was more pronounced in women, and in overweight or obese subjects. The relation of lutein/zeaxanthin to RCC was stronger in ever smokers. No clear association was observed with vitamin C and E, beta-cryptoxanthin, and lycopene.

**CONCLUSION:** The findings provide evidence that a diet rich in beta-carotene and lutein/zeaxanthin may play a role in RCC prevention.

## GASTROINTESTINAL CANCER

Jiang, ZM, D. W. Wilmore, X. R. Wang, et al.

### **Randomized Clinical Trial of Intravenous Soybean Oil Alone Versus Soybean Oil Plus Fish Oil Emulsion After Gastrointestinal Cancer Surgery.**

*Br J Surg.* 2010 Jun; 976: 804-809.

**BACKGROUND:** Specific immunonutrients may reduce the incidence of postoperative complications and



shorten recovery time. This randomized trial evaluated the clinical efficacy of a fish oil emulsion on outcome and immune function after gastrointestinal cancer surgery. **METHODS:** A total of 206 patients with gastrointestinal or colonic cancer were randomized to receive isocaloric and isonitrogenous intravenous infusions of either soybean oil alone (1.2 g per kg bodyweight per day; control group, 103 analysed) or soybean plus fish oil emulsion (1.0 and 0.2 g per kg per day respectively; treatment group, 100 analysed) over 20-24 h daily for 7 days after surgery.

**RESULTS:** Baseline data were comparable in the two groups. There were fewer infectious complications (four versus 12 on day 8;  $P = 0.066$ ), systemic inflammatory response syndrome (SIRS) was significantly less common (four versus 13;  $P = 0.039$ ) and hospital stay was significantly shorter (mean(s.d.) 15(5) versus 17(8) days;  $P = 0.041$ ) in the treatment group. Total postoperative medical costs were comparable in the two groups (mean (s.d.) US \$ 1269(254) and 1302(324) in treatment and control groups respectively;  $P = 0.424$ ). The median (interquartile range) difference in CD4/CD8 between days 1 and 8 after surgery was + 0.30 (0.06 to 0.79) in patients receiving fish oil and + 0.20 (-0.19 to 0.55) in controls ( $P = 0.021$ ). No severe adverse events occurred in either group.

**CONCLUSION:** Fish oil emulsion-supplemented parenteral nutrition significantly reduced SIRS and length of hospital stay. These clinical benefits may be related to normalization of cellular immune functions and modulation of the inflammatory response.

## GYNECOLOGICAL CANCERS

Karageorgi, S, M. A. Gates, S. E. Hankinson et al.

### Perineal use of Talcum Powder and Endometrial Cancer Risk.

*Cancer Epidemiology Biomarkers and Prevention.* 2010 May; 195: 1269-1275.

**BACKGROUND:** Several studies have reported a positive association between perineal use of talcum powder among adult women and ovarian cancer risk. However, the relationship between talcum powder use and other gynecologic malignancies such as endometrial cancer has not been examined, and little information is available on nonhormonal risk factors for endometrial cancer. **METHODS:** Perineal use of talcum powder was assessed in 1982 in the Nurses' Health Study. Approximately 40% of women who responded to the questions about perineal use of talcum powder reported ever use. Cox proportional hazards models were used to estimate the incidence rate ratio of endometrial cancer and 95% confidence interval (CI), adjusted for body mass index and other potential confounders. We evaluated the relationship among all women and stratified by menopausal status.

**RESULTS:** Our analysis included 66,028 women with 599 incident cases of invasive endometrial adenocarcinoma diagnosed between 1982 and 2004. Although no association was observed overall, the association varied by menopausal status ( $P$  interaction = 0.02) and a positive association was observed among postmenopausal women; ever use of talcum powder was associated with a 21% increase in risk of endometrial cancer (95% CI, 1.02-1.44), whereas regular use (at least once a week) was associated with a 24% increase in risk (95% CI, 1.03-1.48). In addition, we observed a borderline increase in risk with increasing frequency of use ( $P$  trend = 0.04).

**CONCLUSIONS:** Our results suggest that perineal talcum powder use increases the risk of endometrial cancer, particularly among postmenopausal women. **IMPACT:** Future and larger studies are needed to confirm this association and investigate potential mechanisms.

## HODGKIN'S LYMPHOMA

Kiserud, CE, J. H. Loge, A. Fossa, et al.

### Mortality is Persistently Increased in Hodgkin's Lymphoma Survivors.

*Eur J Cancer.* 2010 June; 469: 1632-1639.

**BACKGROUND:** Negative health outcomes of chronic fatigue (CF) in disease-free cancer survivors are mainly unexplored. Aims of this study were to examine mortality and causes of death in Hodgkin's lymphoma survivors (HLSs) compared to controls from the general population, and to explore if CF was



associated with increased mortality. **METHODS:** HLSs (n = 557) invited to participate in a survey on late effects in 1994 were divided into three groups: participants without CF (n = 329), participants with CF (n = 113), non-participants (n = 98). Controls matched for gender and age were drawn from the general population (five per HLSs, n = 2785). Observation time was calculated from 1st January 1994 until date of death or cut-off at 1st January 2007. Kaplan-Meier plots were used for univariate analyses and Cox models for multiple covariates.

**RESULTS:** Compared to controls HLSs had nearly five times higher mortality (HR = 4.93; 95% confidence interval [CI]: 3.91-6.21) and the mortality rate of HLSs was higher than the rate of their controls for the entire observation period. Mortality was increased in all groups: participants with CF: HR = 4.85 (95% CI: 3.02-7.77), participants without CF: HR = 4.35 (95% CI: 3.16-6.00), non-participants: HR = 9.45 (95% CI: 5.44-16.41). Compared to the controls HLSs had over six times increased mortality of cancer (HR: 6.6, 95% CI: 4.7-9.2) and almost five times increased mortality of cardiovascular diseases (HR: 4.9, 95% CI: 3.1-7.9).

**CONCLUSIONS:** HLSs had almost five-time increased mortality compared to controls. CF was not associated with increased mortality rate. The high mortality among the non-participating HLSs indicates that serious health problems are underestimated in this group. This has implications for the interpretation of surveys in cancer survivors.

## MELATONIN

Nahleh, Z, J. Pruemer, J. Lafollette et al.

### Melatonin, a Promising Role in Taxane-Related Neuropathy.

*Clinical Medicine Insights: Oncology.* 2010 4pp 35-41: ate of Pubaton: 2010.

**PURPOSE:** Melatonin has neuroprotective effects in animal studies and has been suggested to decrease adverse reactions of chemotherapy including neuropathy. This pilot trial aimed at assessing whether melatonin, given during taxane chemotherapy for breast cancer, will decrease the incidence and/or severity of neuropathy. **METHODS:** Twenty two consecutive patients beginning chemotherapy for breast cancer with paclitaxel, or docetaxel were enrolled. Patients received melatonin 21 mg daily at bedtime. Incidence and severity of neuropathy were assessed using neurological examinations, toxicity assessment per NCI-CTC 3.0 scale and FACT-Taxane quality of life questionnaire.

**RESULTS:** Neuropathy was seen in 45% (n = 10) of patients, 23% (n = 6) grade 1 and 22% (n = 5) Grade 2 neuropathy. No grade 3 neuropathies were reported. The majority (55%) of all patients reported no neuropathy. Compliance with melatonin (>60% of dose) was seen in most patients (86%) No patient reported daytime sedation. The median FACT-Taxane quality of life end of study score was 137, with only a 0.5 median decline from baseline.

**CONCLUSION:** Patients receiving melatonin during taxane chemotherapy had a reduced incidence of neuropathy. Melatonin may be useful in the prevention or reduction of taxane-induced neuropathy and in maintaining quality of life. Larger trials are warranted to further explore the role of melatonin in neuropathy treatment and prevention.

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