



# RESEARCH UPDATES

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## Nutrition

Epplein, M, A. A. Franke, R. V. Cooney, et al. **Association of Plasma Micronutrient Levels and Urinary Isoprostane with Risk of Lung Cancer: The Multiethnic Cohort Study.** *Cancer Epidemiology, Biomarkers & Prevention.* 2009 Jul; 187: 1962-1970.

Although smoking is the primary risk factor for lung cancer, there is evidence to suggest that fruit and vegetable intake are important cofactors. The present case-control study, nested within the Multiethnic Cohort Study, examined the associations of biomarkers of fruit and vegetable intake (individual plasma micronutrient levels), serum selenium, and a urinary biomarker for total lipid peroxidation with lung cancer risk. Two hundred seven incident cases were matched to 414 controls on age, sex, ethnicity, study location (Hawaii or California), smoking status, date/time of collection, and hours of fasting. We measured prediagnostic circulating levels of individual tocopherols and carotenoids, retinol, and serum selenium, and urinary 15-isoprostane F(2t). Conditional logistic regression was used to compute odds ratios (OR) and 95% confidence intervals (CI). For men, strong reductions in risk were seen with increasing tertiles of each plasma carotenoid, with the ORs for the third tertile, compared with the first tertile, ranging from 0.24 to 0.45 (P(trends), 0.002-0.04). No associations were found among women for carotenoids or among either sex for tocopherols, selenium, and retinol. A doubling in risk was seen for men in the second and third tertiles, compared with the first tertile of urinary 15-isoprostane F(2t) (OR, 2.31; 95% CI, 1.02-5.25; and OR, 2.16; 95% CI, 0.98-4.78). This study supports the

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previously observed association between circulating carotenoids and lung cancer risk in men, and adds to the limited literature regarding urinary 15-isoprostane F(2t) as a marker of cancer risk. Future research examining the possible relationship between isoprostanes and lung cancer is warranted.

## Colorectal Cancer

Soler-Vila, H, R. Dubrow, V. I. Franco, A. K. Saathoff, S. V. Kasl and B. A. Jones. **Cancer-Specific Beliefs and Survival in Nonmetastatic Colorectal Cancer Patients.** *Cancer.* 2009 15 Sep; 115SUPPL. 18: 4270-4282.

**BACKGROUND:** Colorectal cancer (CRC) is the third leading cause of cancer mortality in the United States. Associations between cancer-specific beliefs (beliefs) and survival have been observed among other cancer populations, but similar research in CRC patients is virtually nonexistent, especially in racially diverse populations. The relationship between beliefs and survival was investigated in a cohort of African Americans and non-Hispanic whites with newly diagnosed nonmetastatic CRC, followed for up to 15 years. **METHODS:** The authors analyzed data from a population-based cohort of 286 individuals (115 African Americans and 171 whites, approximately 52% women) diagnosed with nonmetastatic CRC in Connecticut, 1987 to 1991. Cox proportional hazards models were adjusted for sociodemographic (age, sex, race, education, income, occupational status, marital status) and biomedical (stage at diagnosis, histological grade, treatment) variables. **RESULTS:** Not believing in the curability of cancer increased the risk of all-cause mortality (hazard ratio [HR], 1.59; 95% confidence interval [CI], 1.06-2.39) and CRC-specific mortality (HR, 1.65; 95% CI, 0.90-3.03; P = .10). These multivariate estimates were not altered by additional adjustment

for insurance coverage, obesity, smoking, alcohol consumption, or comorbidity. Furthermore, the association between perceived curability and survival did not vary significantly by key sociodemographic or biomedical factors. Other beliefs were not associated with survival. **CONCLUSIONS:** Among a racially diverse cohort of men and women with CRC, believing in the curability of cancer was independently associated with survival over a 15-year period. Confirmation of the role of cancer-specific beliefs on survival and study of the potential biobehavioral mechanisms is needed. Findings may inform the design of interventions for cancer survivors.

Stein, KD, C. Kaw, C. Cramer and T. Gansler. **The Role of Psychological Functioning in the use of Complementary and Alternative Methods among Disease-Free Colorectal Cancer Survivors: A Report from the American Cancer Society's Studies of Cancer Survivors.** *Cancer.* 2009 15 Sep; 115SUPPL. 18: 4397-4408.

**BACKGROUND:** The medical and demographic correlates of complementary and alternative medicine (CAM) use among cancer survivors have been well documented. However, the role of psychological functioning in cancer survivors' CAM use and the degree to which such factors apply to survivors of colorectal cancer require additional study. In addition, sex differences in CAM use and its correlates among colorectal cancer survivors are not well understood. **METHODS:** By using data from a large-scale national population-based study of quality of life and health behaviors among cancer survivors, the authors examined the prevalence and psychological correlates of CAM use among 252 male and 277 female colorectal cancer survivors. **RESULTS:** Use of CAM was more common among women, those with more education, and recipients of chemotherapy and radiation therapy. Several psychological factors predicted increased use of CAM among female colorectal cancer survivors, including anxiety, fear of cancer recurrence, fatigue, vigor, anger, mental confusion, and overall emotional distress. Depression was associated with decreased CAM use among female survivors, both for overall CAM use and across several standard CAM domains. In contrast, psychological functioning had little impact on male colorectal cancer survivors' CAM use. The only nonmedical/demographic variable associated with men's use of CAM was fatigue, which predicted use only of biologically based practices, such as diet and nutritional supplements. **CONCLUSIONS:** Psychological functioning has a significant impact on CAM use among female colorectal cancer survivors. Decreased use of CAM among women with depressive symptoms was unexpected and warrants additional investigation.

## Breast Cancer

Obi, N, J. Chang-Claude, J. Berger, et al. **The use of Herbal Preparations to Alleviate Climacteric Disorders and Risk of Postmenopausal Breast Cancer in a German Case-Control Study.** *Cancer Epidemiology, Biomarkers & Prevention.* 2009 Aug; 188: 2207-2213.

**BACKGROUND:** The use of herbal preparations (HEP) to alleviate climacteric disorders is expected to increase as women seek alternatives to menopausal hormone therapy to avoid the associated breast cancer risk. Data are sparse on the long-term effects of HEP containing phytoestrogens

and black cohosh on breast cancer risk. **METHODS:** Within a German case-control study, associations between patterns of HEP use and incident breast cancer were investigated in 10,121 postmenopausal women (3,464 cases, 6,657 controls). Information on HEP use was collected in face-to-face interviews supported by a list of brand names. Multivariate logistic and polytomous regression analyses were done. **FINDINGS:** Ever use of HEP (9.9%) was inversely associated with invasive breast cancer [odds ratio (OR), 0.74; 95% confidence interval (CI), 0.63-0.87] in a dose-dependent manner (OR, 0.96 per year of use;  $P = 0.03$ ). Classes of HEP did not differ significantly ( $P(\text{heterogeneity}) = 0.81$ ). Risks for invasive ductal (OR, 0.72; 95% CI, 0.60-0.87) and combined lobular/mixed/tubular tumors (OR, 0.76; 95% CI, 0.58-1.01) were similarly reduced by any HEP use but not for in situ carcinomas (1.34; 95% CI, 0.86-2.09). There were no substantial differences in associations of HEP use by estrogen receptor status (ER(+)) OR, 0.74; 95% CI, 0.62-0.89; ER- OR, 0.68, 95% CI, 0.50-0.93) and progesterone receptor status of the tumor. **INTERPRETATION:** Our findings support the hypothesis that HEP use protects from invasive breast cancer in postmenopausal women. Among conceivable modes of action, those independent of estrogen receptor-mediated pathways seem to be involved (i.e., cytotoxicity, apoptosis).

Park, Y, L. A. Brinton, A. F. Subar, A. Hollenbeck and A. Schatzkin. **Dietary Fiber Intake and Risk of Breast Cancer in Postmenopausal Women: The National Institutes of Health-AARP Diet and Health Study.** *Am J Clin Nutr.* 2009 Sep; 90(3): 664-671.

**BACKGROUND:** Although dietary fiber has been hypothesized to lower risk of breast cancer by modulating estrogen metabolism, the association between dietary fiber intake and risk of breast cancer by hormone receptor status is unclear. **OBJECTIVE:** The objective was to examine the relation of dietary fiber intake to breast cancer by hormone receptor status and histologic type among postmenopausal women in the National Institutes of Health-AARP Diet and Health Study ( $n = 185,598$ ; mean age: 62 y). **DESIGN:** Dietary intakes were assessed with a food-frequency questionnaire. Incident breast cancer cases were identified through linkage with state cancer registries. Cox proportional hazard models were used to estimate relative risks (RRs) and 2-sided 95% CIs. **RESULTS:** During an average of 7 y of follow-up, 5461 breast cancer cases were identified, of which 3341 cases had estrogen receptor (ER) and progesterone receptor (PR) status. Dietary fiber intake was inversely associated with breast cancer risk [RR for the highest quintile (Q5) compared with the lowest quintile (Q1): 0.87; 95% CI: 0.77, 0.98;  $P$  for trend: 0.02]. The inverse association appeared to be stronger for ER(-)/PR(-) tumors (RR(Q5vsQ1): 0.56; 95% CI: 0.35, 0.90;  $P$  for trend: 0.008; 366 cases) than for ER(+)/PR(+) tumors (RR(Q5vsQ1): 0.95; 95% CI: 0.76, 1.20;  $P$  for trend: 0.47; 1641 cases). The RR(Q5vsQ1) of lobular tumors was 0.66 (95% CI: 0.44, 0.97;  $P$  for trend: 0.04), and the RR(Q5vsQ1) of ductal tumors was 0.90 (95% CI: 0.77, 1.04;  $P$  for trend: 0.10). Fiber from grains, fruit, vegetables, and beans was not related to breast cancer. **CONCLUSION:** Our findings suggest that dietary fiber can play a role in preventing breast cancer through nonestrogen pathways among postmenopausal women.

## Prostate Cancer

Fradet, V, I. Cheng, G. Casey and J. S. Witte. **Dietary Omega-3 Fatty Acids, Cyclooxygenase-2 Genetic Variation, and Aggressive Prostate Cancer Risk.** *Clinical Cancer Research.* 2009 Apr 1; 157: 2559-2566.

**PURPOSE:** Dietary intake of long-chain omega-3 (LC n-3) polyunsaturated fatty acids may reduce inflammation and in turn decrease risk of prostate cancer development and progression. This potential effect may be modified by genetic variation in cyclooxygenase-2 (COX-2), a key enzyme in fatty acid metabolism and inflammation. **EXPERIMENTAL DESIGN:** We used a case-control study of 466 men diagnosed with aggressive prostate cancer and 478 age- and ethnicity-matched controls. Diet was assessed with a semiquantitative food frequency questionnaire, and nine COX-2 tag single nucleotide polymorphisms (SNP) were genotyped. We used logistic regression models to estimate odds ratios (OR) for association and interaction. **RESULTS:** Increasing intake of LC n-3 was strongly associated with a decreased risk of aggressive prostate cancer ( $P(\text{trend}) < 0.0001$ ). The OR (95% confidence interval) for prostate cancer comparing the highest with the lowest quartile of n-3 intake was of 0.37 (0.25-0.54). The LC n-3 association was modified by SNP rs4648310 (+8897 A/G), flanking the 3' region of COX-2 ( $P(\text{interaction}) = 0.02$ ). In particular, the inverse association was even stronger among men with this variant SNP. This reflected the observation that men with low LC n-3 intake and the variant rs4648310 SNP had an increased risk of disease (OR, 5.49; 95% confidence interval, 1.80-16.7), which was reversed by increasing intake of LC n-3. **CONCLUSIONS:** Dietary LC n-3 polyunsaturated fatty acids appear protective for aggressive prostate cancer, and this effect is modified by the COX-2 SNP rs4648310. Our findings support the hypothesis that LC n-3 may impact prostate inflammation and carcinogenesis through the COX-2 enzymatic pathway.

Trump, DL, M. K. Chadha, A. Y. Sunga, et al. **Vitamin D Deficiency and Insufficiency among Patients with Prostate Cancer.** *BJU Int.* 2009 October; 1047: 909-914.

**Objective:** To assess the frequency of vitamin D deficiency among men with prostate cancer, as considerable epidemiological, in vitro, in vivo and clinical data support an association between vitamin D deficiency and prostate cancer outcome. **Patients, Subjects and Methods:** The study included 120 ambulatory men with recurrent prostate cancer and 50 with clinically localized prostate cancer who were evaluated and serum samples assayed for 25-OH vitamin D levels. Then 100 controls (both sexes), matched for age and season of serum sample, were chosen from a prospective serum banking protocol. The relationship between age, body mass index, disease stage, Eastern Cooperative Oncology Group performance status, season and previous therapy on vitamin D status were evaluated using univariate and multivariate analyses. **Results:** The mean 25-OH vitamin D level was 25.9 ng/mL in those with recurrent disease, 27.5 ng/mL in men with clinically localized prostate cancer and 24.5 ng/mL in controls. The frequency of vitamin D deficiency (<20 ng/mL) and insufficiency (20-31 ng/mL) was 40% and 32% in men with recurrent prostate; 28% had vitamin D

levels that were normal (32-100 ng/mL). Among men with localized prostate cancer, 18% were deficient, 50% were insufficient and 32% were normal. Among controls, 31% were deficient, 40% were insufficient and 29% were normal. Metastatic disease ( $P = 0.005$ ) and season of blood sampling (winter/spring;  $P = 0.01$ ) were associated with vitamin D deficiency in patients with prostate cancer, while age, race, performance status and body mass index were not. **Conclusions:** Vitamin D deficiency and insufficiency were common among men with prostate cancer and apparently normal controls in the western New York region.

We are grateful to the **Prostate Cancer Foundation BC** for their generous support.



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## Caregiving

Yabroff, KR and Y. Kim. **Time Costs Associated with Informal Caregiving for Cancer Survivors.** *Cancer.* 2009 15 Sep; 115SUPPL. 18: 4362-4373.

**BACKGROUND:** To the authors' knowledge, little work has been done to estimate the time costs associated with informal caregiving for cancer survivors. **METHODS:** Data from a national survey of caregivers of cancer patients in 2003 to 2006 were used to estimate the time associated with informal caregiving in the 2 years after patient diagnosis with bladder, breast, colorectal, kidney, lung, melanoma of the skin, ovarian, prostate, or uterine cancer, or non-Hodgkins lymphoma (NHL). Caregivers reported the duration and daily intensity of caregiving as well as the types and frequency of support provided. The median wage rate in 2006 (\$16.28) was used to value caregiver time, and other methods to value time were evaluated with sensitivity analyses. **RESULTS:** On average, caregivers provided care for 8.3 hours per day for 13.7 months. The number of months and daily hours spent caregiving were the highest for cancer survivors diagnosed with distant disease compared with survivors with regional or localized disease ( $P < .05$ ). Approximately half of caregivers provided emotional, instrumental, tangible, or medical support, although the frequency varied dramatically. Informal caregiver time costs over the 2-year period after diagnosis were the highest for caregivers of patients diagnosed with lung (\$72,702; 95% confidence interval [95% CI], \$56,814-\$88,590) and ovarian (\$66,210; 95% CI, \$40,750-\$91,670) cancers and NHL (\$59,613; 95% CI, \$43,423-\$75,803) and the lowest for caregivers of patients with breast cancer (\$38,334; 95% CI, \$31,442-\$45,226). **CONCLUSIONS:** Time spent by informal caregivers was substantial and was an important component of the burden of cancer care. Incorporation of the value of informal caregiver time will be important when evaluating the costs and benefits of cancer control interventions.

Magill, L **The Spiritual Meaning of Pre-Loss Music Therapy to Bereaved Caregivers of Advanced Cancer Patients.** *Palliative & Supportive Care.* 2009 Mar; 71: 97-108.

**OBJECTIVE:** The aim of this study was to learn how music therapy sessions, held prior to the death of a loved one, impact spirituality in surviving caregivers of advanced cancer patients. **METHOD:** The method of naturalistic inquiry was used to investigate the spiritual meaning of pre-loss music therapy sessions. Bereaved caregivers of seven different patients, who had been receiving music therapy through a home-based hospice program, participated in individual open-ended interviews. Interviews were recorded, transcribed, and coded. Themes were organized as they emerged. **RESULTS:** As caregivers reflected on their experiences in music therapy, they reported autonomous joy (music therapy affected the caregiver directly) and empathic joy (caregivers' joy was based in remembering seeing the patient happy in music therapy). They also noted feelings of empowerment due to the ways they felt they had contributed in the care of the patients through music therapy. The caregivers were found to engage in processes of reflection that inspired these spiritual themes: reflection on the present (connectedness), reflection on the past (remembrance), and reflection on the future (hope). They referred to the ways that the music therapy sessions helped them find connection with self, others (through bringing their loved ones "back to life" and have a "renewal of self"), and the "beyond"; and that times in music therapy brought them happy memories and sentiments of hope. Meaning through transcendence was found to be the overarching trend in this study, as caregivers were lifted from remorse into heightened sense of meaning and gained "airplane views" of their lives. **SIGNIFICANCE OF RESULTS:** Pre-loss music therapy can potentially assist caregivers during times of bereavement, as they retain memories of joy and empowerment, rather than memories of pain and distress, and find meaning through transcendence.

Porter, LS, F. J. Keefe, D. H. Baucom, et al. **Partner-Assisted Emotional Disclosure for Patients with Gastrointestinal Cancer: Results from a Randomized Controlled Trial.** *Cancer.* 2009 15 Sep; 115SUPPL. 18: 4326-4338.

**BACKGROUND:** For patients with cancer who are married or in an intimate relationship, their relationships with their partners play a critical role in their adaptation to illness. However, cancer patients and their partners often have difficulty in talking with each other about their cancer-related concerns. Difficulties in communication ultimately may compromise both the patient-partner relationship and the patient's psychological adjustment. The current study tested the efficacy of a novel partner-assisted emotional disclosure intervention in a sample of patients with gastrointestinal (GI) cancer. **METHODS:** One hundred thirty patients with GI cancer and their partners were assigned randomly to receive 4 sessions of either partner-assisted emotional disclosure or a couples cancer education/support intervention. Patients and partners completed measures of relationship quality, intimacy with their partner, and psychological distress before randomization and at the end of the intervention sessions. Data were analyzed using multilevel modeling. **RESULTS:** Compared with an education/support condition, the partner-assisted emotional disclosure condition led to improvements in relationship quality and intimacy for couples in which the patient initially reported higher levels of holding back from discussing cancer-related concerns.

**CONCLUSIONS:** Partner-assisted emotional disclosure is a novel intervention that builds on both the private emotional disclosure and the cognitive-behavioral marital literature. The results of this study suggested that this intervention may be beneficial for couples in which the patient tends to hold back from discussing concerns. The authors concluded that future research on methods of enhancing the effects of partner-assisted emotional disclosure is warranted.

## Study of the Month

Schmitz, KH, R. L. Ahmed, A. Troxel, et al. **Weight Lifting in Women with Breast-Cancer-Related Lymphedema.** *N Engl J Med.* 2009 13 Aug; 3617: 664-673.

**BACKGROUND:** Weight lifting has generally been proscribed for women with breast-cancer-related lymphedema, preventing them from obtaining the well-established health benefits of weight lifting, including increases in bone density. **METHODS:** We performed a randomized, controlled trial of twice-weekly progressive weight lifting involving 141 breast-cancer survivors with stable lymphedema of the arm. The primary outcome was the change in arm and hand swelling at 1 year, as measured through displaced water volume of the affected and unaffected limbs. Secondary outcomes included the incidence of exacerbations of lymphedema, number and severity of lymphedema symptoms, and muscle strength. Participants were required to wear a well-fitted compression garment while weight lifting. **RESULTS:** The proportion of women who had an increase of 5% or more in limb swelling was similar in the weight-lifting group (11%) and the control group (12%) (cumulative incidence ratio, 1.00; 95% confidence interval, 0.88 to 1.13). As compared with the control group, the weight-lifting group had greater improvements in self-reported severity of lymphedema symptoms ( $P = 0.03$ ) and upper- and lower-body strength ( $P < 0.001$  for both comparisons) and a lower incidence of lymphedema exacerbations as assessed by a certified lymphedema specialist (14% vs. 29%,  $P = 0.04$ ). There were no serious adverse events related to the intervention. **CONCLUSIONS:** In breast-cancer survivors with lymphedema, slowly progressive weight lifting had no significant effect on limb swelling and resulted in a decreased incidence of exacerbations of lymphedema, reduced symptoms, and increased strength. (ClinicalTrials.gov number, NCT00194363).

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