



# REsearch UPDATES

FOR THE LATEST IN WORLDWIDE INTEGRATIVE CANCER CARE

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**IN THIS ISSUE:** Tomaszewski et al. found a link between folate metabolism and prostate cancer. Djuric and colleagues reported on a lifestyle intervention that was beneficial and feasible for women with breast cancer on chemotherapy. Bourke and associates reported similar findings on a diet and exercise intervention for people with colon cancer. Hajizadeh and colleagues discovered that fruit reduced the risk of esophageal squamous cell carcinoma. Johnston et al. found patient education and acupuncture to be beneficial for cancer patients suffering from cancer-related fatigue. Meraviglia and Stuijbergen indicated that low-income cancer survivors tend to engage in health-promoting behaviours and are likely to want more information after cancer treatment. Park and associates reported that dietary fiber reduced the risk of death from cancer for men. In our study of the month, Noji and Takayanagi reported about a woman with advanced gastric cancer whose case provided evidence for the adage, "laughter is the best medicine."

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## PROSTATE CANCER

Tomaszewski, JJ, J. L. Cummings, A. V. Parwani, et al.

### Increased Cancer Cell Proliferation in Prostate Cancer Patients with High Levels of Serum Folate.

*Prostate*. 2011 Sept 2011;7112: 1287-1293.

**BACKGROUND:** A recent clinical trial revealed that folic acid supplementation is associated with an increased incidence of prostate cancer (Figueiredo et al., *J Natl Cancer Inst* 2009; 101(6): 432-435). As tumor cells in culture proliferate directly in response to available folic acid, the goal of our study was to determine if there is a similar relationship between patient folate status, and the proliferative capacity of tumors in men with prostate cancer. **METHODS:** Serum folate and/or prostate tissue folate was determined in 87 randomly selected patients undergoing surgery for prostate cancer, and compared to tumor proliferation in a subset.

**RESULTS:** Fasting serum folate levels were positively correlated with prostate tumor tissue folate content ( $n = 15$ ;  $r = 0.577$ ,  $P < 0.03$ ). Mean serum folate was 62.6 nM (7.5-145.2 nM), 39.5% of patients used supplements containing folic acid ( $n = 86$ ). The top quartile of patients had serum folates above 82 nM, six times the level considered adequate. Of these, 48% reported no supplement use. Among 50 patients with Gleason 7 disease, the mean proliferation index as determined by Ki67 staining was 6.17 A+/- 3.2% and 0.86 A+/- 0.92% in the tumors from patients in the highest (117 A+/- 15 nM) and lowest (18 A+/- 9 nM) quintiles for serum folate, respectively ( $P < 0.0001$ ).

**CONCLUSIONS:** Increased cancer cell proliferation in men with higher serum folate concentrations is consistent with an increase in prostate cancer incidence observed with folate supplementation. Unexpectedly, more than 25% of patients had serum folate levels greater than sixfold adequate. Nearly half of these men reported no supplement use, suggesting either altered folate metabolism and/or sustained consumption of folic acid from fortified foods.

## BREAST CANCER

Djuric, Z, J. S. Ellsworth, A. L. Weldon, et al.

### A Diet and Exercise Intervention during Chemotherapy for Breast Cancer.

*Open Obesity Journal*. 2011 2011; 387-97.

**BACKGROUND:** Weight gain is an important concern that impacts on breast cancer outcomes and general health in survivorship. This randomized, pilot study evaluated whether or not women could comply with a weight control program that is initiated at the beginning of chemotherapy for breast cancer. **METHODS:** The program sought to prevent weight gain using a low-fat, high fruit-vegetable diet combined with moderate physical activity. The intervention was implemented using a telephone counseling approach that blended motivational interviewing with social cognitive theory. A total of 40 women were recruited over 9 months at the University of Michigan Comprehensive Cancer Center. This represents 55% of eligible women referred to the study and indicates that interest in a healthy lifestyle program at the initiation of chemotherapy for breast cancer was high. Subjects who dropped out had significantly lower fruit and vegetable intakes and lower blood carotenoids at baseline than subjects who completed the study.

**RESULTS:** Statistically significant beneficial effects were observed on fruit and vegetable intakes, physical activity and breast cancer-specific well-being by the intervention. Mean body fat from dual energy X-ray absorptiometry increased in the written materials arm and decreased in the intervention arm. Of the enrolled women, 75% completed 12 months on study and satisfaction with study participation was high.

**CONCLUSION:** These data indicate that lifestyle intervention during breast cancer treatment is feasible during treatment with chemotherapy for breast cancer and benefits women in several domains.



## COLON CANCER

Bourke, L, G. Thompson, D. J. Gibson, et al.

### Pragmatic Lifestyle Intervention in Patients Recovering from Colon Cancer: A Randomized Controlled Pilot Study.

*Archives of Physical Medicine & Rehabilitation.* 2011 May;925:749-755.

**OBJECTIVE:** To investigate the feasibility of a pragmatic lifestyle intervention in patients who had recently completed surgery and chemotherapy for colon cancer and to obtain preliminary data of its impact on important health outcomes. **DESIGN:** A prospective, randomized, controlled pilot trial. **SETTING:** University rehabilitation facility. **PARTICIPANTS:** Eighteen (N=18) colon cancer survivors (mean age=69y; range, 52-80y), Dukes stage A to C. **INTERVENTIONS:** Participants were randomized 6 to 24 months postoperatively to either a 12-week program of combined exercise and dietary advice or standard treatment. **MAIN OUTCOME MEASURES:** Exercise and dietary behavior, fatigue, health-related quality of life (QOL), aerobic exercise tolerance, functional capacity, muscle strength, and anthropometry were assessed at baseline and immediately after the intervention.

**RESULTS:** Adherences to supervised and independent exercise during the intervention were 90% and 94%, respectively, and there was low attrition (6%). The lifestyle intervention elicited improvements in exercise behavior (P=.068), fatigue (P=.005), aerobic exercise tolerance (P=.010), chair sit-to-stand performance (P=.003), and waist-to-hip ratio (P=.002). A positive change in dietary fiber intake (P=.044) was also observed in the intervention group. No change in QOL was observed (P=.795).

**CONCLUSIONS:** These preliminary results suggest that a pragmatic lifestyle intervention implemented 6 to 24 months after primary treatment for colon cancer was feasible. We observed a significant impact on dietary behavior, fatigue, aerobic exercise tolerance, functional capacity, and waist-to-hip ratio. These findings need to be confirmed with a larger-scale definitive randomized controlled trial.

## CAM USE IN ONCOLOGY

Chang, KH, R. Brodie, M. A. Choong, et al.

### Complementary and Alternative Medicine use in Oncology: A Questionnaire Survey of Patients and Health Care Professionals.

*BMC Cancer.* 2011 24 May 2011; 11

**BACKGROUND:** We aimed to investigate the prevalence and predictors of Complementary and Alternative Medicine (CAM) use among cancer patients and non-cancer volunteers, and to assess the knowledge of and attitudes toward CAM use in oncology among health care professionals. **METHODS:** This is a cross-sectional questionnaire survey conducted in a single institution in Ireland. Survey was performed in outpatient and inpatient settings involving cancer patients and non-cancer volunteers. Clinicians and allied health care professionals were asked to complete a different questionnaire.

**RESULTS:** In 676 participants including 219 cancer patients; 301 non-cancer volunteers and 156 health care professionals, the overall prevalence of CAM use was 32.5% (29.1%, 30.9% and 39.7% respectively in the three study cohorts). Female gender ( $p < 0.001$ ), younger age ( $p = 0.004$ ), higher educational background ( $p < 0.001$ ), higher annual household income ( $p = 0.001$ ), private health insurance ( $p = 0.001$ ) and non-Christian ( $p < 0.001$ ) were factors associated with more likely CAM use. Multivariate analysis identified female gender ( $p < 0.001$ ), non-Christian ( $p = 0.001$ ) and private health insurance ( $p = 0.015$ ) as independent predictors of CAM use. Most health care professionals thought they did not have adequate knowledge (58.8%) nor were up to date with the best evidence (79.2%) on CAM use in oncology. Health care professionals who used CAM were more likely to recommend it to patients ( $p < 0.001$ ).

**CONCLUSIONS:** This study demonstrates a similarly high prevalence of CAM use among oncology health care professionals, cancer and non cancer patients. Patients are more likely to disclose CAM usage if they are specifically asked. Health care professionals are interested to learn more about various CAM therapies and have poor evidence-based knowledge on specific oncology treatments. There is a need for further training to meet to the escalation of CAM use among patients and to raise awareness of potential benefits and risks associated with these therapies.

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## ESOPHAGEAL SQUAMOUS CELL CARCINOMA

Hajizadeh, B, M. Jessri, S. M. Moasheri, et al.

### Fruits and Vegetables Consumption and Esophageal Squamous Cell Carcinoma: A Case-Control Study.

*Nutr Cancer.* 2011 July 2011;635: 707-713.

**BACKGROUND:** The authors examined the association of food group intakes and the risk of esophageal squamous cell carcinoma (SCC) in a hospital-based case-control study in Iran. **METHODS:** In total, 47 patients with esophageal SCC and 96 controls underwent face-to-face private interviews. Usual dietary intake was assessed using a semiquantitative food frequency questionnaire. Multivariate logistic regression was used to estimate odds ratios and 95% confidence intervals.

**RESULTS:** Cases had higher tobacco consumption and symptomatic gastresophageal reflux, whereas controls had higher mean body mass index (25.3 vs. 20.4) and years of education. A protective independent effect was observed for the highest tertile of total fruit consumption (OR: 0.13, CI: 0.04-0.45, P value = 0.001). Within the group of fruits, a significant inverse association was observed for bananas and kiwis (P for trends: 0.03 and 0.02, respectively). The risk of SCC decreased monotonically with increasing intake frequency of oranges (P value for trend = 0.01). The effect of total vegetable consumption on esophageal SCC was not significant, although a reduction in risk was observed in the highest tertile of intake (OR: 0.66, CI: 0.23-1.87, P value = 0.43).

**CONCLUSION:** The results of the present study suggest a reasonable association between fruit consumption and esophageal SCC in a Middle Eastern high-risk population.

## ACUPUNCTURE

Johnston, MF, R. D. Hays, S. K. Subramanian, et al.

### Patient Education Integrated with Acupuncture for Relief of Cancer-Related Fatigue Randomized Controlled Feasibility Study.

*BMC Complementary and Alternative Medicine.* 2011 25 Jun 2011;11

**BACKGROUND:** Cancer-related fatigue (CRF) is a prominent clinical problem. There are calls for multi-modal interventions. **METHODS:** We assessed the feasibility of delivering patient education integrated with acupuncture for relief of CRF in a pilot randomized controlled trial (RCT) with breast cancer survivors using usual care as control. Social cognitive and integrative medicine theories guided integration of patient education with acupuncture into a coherent treatment protocol. The intervention consisted of two parts. First, patients were taught to improve self-care by optimizing exercise routines, improving nutrition, implementing some additional evidence-based cognitive behavioral techniques such as stress management in four weekly 50-minute sessions. Second, patients received eight weekly 50-minute acupuncture sessions. The pre-specified primary outcome, CRF, was assessed with the Brief Fatigue Inventory (BFI). Secondary outcomes included three dimensions of cognitive impairment assessed with the FACT-COGv2.

**RESULTS:** Due to difficulties in recruitment, we tried several methods that led to the development of a tailored recruitment strategy: we enlisted oncologists into the core research team and recruited patients completing treatment from oncology waiting rooms. Compared to usual care control, the intervention was associated with a 2.38-point decline in fatigue as measured by the BFI (90% Confidence Interval from 0.586 to 5.014; p < 0.10). Outcomes associated with cognitive dysfunction were not statistically significant.

**CONCLUSIONS:** Patient education integrated with acupuncture had a very promising effect that warrants conducting a larger RCT to confirm findings. An effective recruitment strategy will be essential for the successful execution of a larger-scale trial. Trial registration: NCT00646633.



## HEALTH PROMOTION

Meraviglia, MG and A. Stuifbergen.

### Health-Promoting Behaviors of Low-Income Cancer Survivors.

*Clinical Nurse Specialist*. 2011 May-Jun; 253: 118-124.

**PURPOSE/OBJECTIVES:** The purpose of this study was to explore the health-promoting (HP) behaviors of low-income cancer survivors before and after their diagnosis of cancer. **DESIGN:** This qualitative study used a purposive sampling strategy to identify low-income, ethnically diverse cancer survivors. **SETTING:** Participants were recruited from an urban outpatient cancer clinic serving only low-income clients. **SAMPLE:** Thirteen, ethnically diverse low-income cancer survivors participated in 60- to 90-minute interviews discussing their experience with HP behaviors before and after their diagnosis with cancer, their cancer experience, and their perspectives on being a cancer survivor. **METHODS:** Conventional content analysis of transcripts and field notes by 2 coders identified words, context, frequency, emphasis, and consistency of participants' comments. Statements were further examined to identify patterns and main themes and to interpret the meaning of what was said.

**FINDINGS:** Participants described their use of various HP behaviors primarily walking, maintaining a positive mental attitude, and changing their diet. Participants discussed their perspectives on having a diagnosis of cancer as well as the meaning of being a cancer survivor. They described spiritual growth through prayer, renewing their faith, maintaining a hopeful outlook, and expressing thankfulness toward God. Participants expressed interested in learning about effective physical exercises, healthy eating, and stress management strategies.

**CONCLUSIONS:** Results suggest that low-income cancer survivors engage in various HP behaviors and want to learn more behaviors to use after cancer treatment. **IMPLICATIONS FOR PRACTICE:** Findings provide useful information for clinical nurse specialists when providing information about HP behaviors for use during and after cancer treatment as well as the meaning of cancer survivor for low-income cancer survivors.

## DIETARY FIBER

Park, Y, A. F. Subar, A. Hollenbeck and A. Schatzkin.

### Dietary Fiber Intake and Mortality in the NIH-AARP Diet and Health Study.

*Arch Intern Med*. 2011 June 27, 2011; 171(12): 1061-1068.

**BACKGROUND:** Dietary fiber has been hypothesized to lower the risk of coronary heart disease, diabetes, and some cancers. However, little is known of the effect of dietary fiber intake on total death and cause-specific deaths. **METHODS:** We examined dietary fiber intake in relation to total mortality and death from specific causes in the NIH (National Institutes of Health)-AARP Diet and Health Study, a prospective cohort study. Diet was assessed using a food-frequency questionnaire at baseline. Cause of death was identified using the National Death Index Plus. Cox proportional hazard models were used to estimate relative risks and 2-sided 95% confidence intervals (CIs).

**RESULTS:** During an average of 9 years of follow-up, we identified 20 126 deaths in men and 11 330 deaths in women. Dietary fiber intake was associated with a significantly lowered risk of total death in both men and women (multivariate relative risk comparing the highest with the lowest quintile, 0.78 [95% CI, 0.73-0.82; P for trend, <.001] in men and 0.78 [95% CI, 0.73-0.85; P for trend, <.001] in women). Dietary fiber intake also lowered the risk of death from cardiovascular, infectious, and respiratory diseases by 24% to 56% in men and by 34% to 59% in women. Inverse association between dietary fiber intake and cancer death was observed in men but not in women. Dietary fiber from grains, but not from other sources, was significantly inversely related to total and cause-specific death in both men and women.

**CONCLUSIONS:** Dietary fiber may reduce the risk of death from cardiovascular, infectious, and respiratory diseases. Making fiber-rich food choices more often may provide significant health benefits.



## COMMUNICATION IN CANCER CARE

Sada, YH, Jr Street, R.L, H. Singh, et al.

### Primary Care and Communication in Shared Cancer Care: A Qualitative Study.

*Am J Manag Care.* 2011 April 2011; 174: 259-265.

**OBJECTIVE:** To explore perceptions of primary care physicians' (PCPs') and oncologists' roles, responsibilities, and patterns of communication related to shared cancer care in 3 integrated health systems that used electronic health records. **STUDY DESIGN:** Qualitative study. **METHODS:** We conducted semistructured interviews with 10 patients having early-stage colorectal cancer and with 14 oncologists and PCPs. Sample sizes were determined by thematic saturation. Dominant themes and codes were identified and subsequently applied to all transcripts.

**RESULTS:** Physicians reported that electronic health records improved communication within integrated systems but that communication with physicians outside of their system was still difficult. Primary care physicians expressed uncertainty about their role during cancer care, although medical oncologists emphasized the importance of comorbidity control during cancer treatment. Patients and physicians described additional roles for PCPs, including psychological distress support and behavior modification counseling.

**CONCLUSIONS:** Integrated systems that use electronic health records likely facilitate shared cancer care through improved PCP-oncologist communication. However, strategies to promote a more active role for PCPs in managing comorbidities, psychological distress, and behavior modification, as well as to overcome communication challenges between physicians not practicing within the same integrated system, are still needed to improve shared cancer care.

## LUNG CANCER

Weinstein, SJ, K. Yu, R. L. Horst, et al.

### Serum 25-Hydroxyvitamin D and Risk of Lung Cancer in Male Smokers: A Nested Case-Control Study.

*PLoS ONE.* 0796 Article Number: e2;6 (6) , 2011ate of Pubaton: 2011.

**BACKGROUND:** A role for vitamin D in cancer risk reduction has been hypothesized, but few data exist for lung cancer. We investigated the relationship between vitamin D status, using circulating 25-hydroxyvitamin D [25(OH)D], and lung cancer risk in a nested case-control study within the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study of Finnish male smokers. **METHODS:** Lung cancer cases (n = 500) were randomly selected based on month of blood collection, and 500 controls were matched to them based on age and blood collection date. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using multivariate-adjusted conditional logistic regression. To account for seasonal variation in 25(OH)D concentrations, season-specific and season-standardized quintiles of 25(OH)D were examined, and models were also stratified on season of blood collection (darker season = November-April and sunnier season = May-October). Pre-determined, clinically-defined cutpoints for 25(OH)D and 25(OH)D as a continuous measure were also examined.

**RESULTS:** Overall, 25(OH)D was not associated with lung cancer. Risks were 1.08 (95% CI 0.67-1.75) and 0.83 (95% CI 0.53-1.31) in the highest vs. lowest season-specific and season-standardized quintiles of 25(OH)D, respectively, and 0.91 (95% CI 0.48-1.72) for the  $\geq 75$  vs.  $\approx 75$  vs.  $< 25$  nmol/L. We also found 11% lower risk for a 10 nmol/L increase in 25(OH)D in the darker season based on the continuous measure (OR = 0.89, 95% CI 0.81-0.98, p = 0.02).

**CONCLUSION:** In this prospective study of male smokers, circulating 25(OH)D was not associated with lung cancer risk overall, although inverse associations were suggested among those whose blood was drawn during darker months.

## STUDY OF THE MONTH

Noji, S and K. Takayanagi.

### A Case of Laughter Therapy that Helped Improve Advanced Gastric Cancer.

*Japan-Hospitals.* 2010 Jul; 29: 59-64.

**BACKGROUND:** We have reported the case of a patient diagnosed as having advanced gastric cancer at the age of 88 years old. An endoscopy revealed a type-2 gastric cancer of 25 x 30 mm in the lesser curvature of the middle stomach body and an Ila gastric cancer with T2 SS and cardiac accessory lesions. Both the type-2 and Ila lesions were defined as tub1 with surrounding atrophic gastritis and entero-epithelium metaplastic carcinoma. **METHODS:** Considering the patient's age and her desire not to receive cancer treatment, we prescribed laughter therapy as recommended by the Society for Healing Environment. The program was implemented in a laughter-inducing environment and consisted of five stages: (1) Making the patient feel safe, (2) Relaxing the patient, (3) Increasing the effectiveness, (4) Improving her condition and (5) Increasing her joy of living.

**RESULTS:** One year and seven months later, an endoscopy of the lesser curvature of the middle stomach body indicated that the lesions clearly improved with a morphological reduction into Ila + Ilc masses. A tissue biopsy revealed that nucleus abnormality clearly improved from the initial diagnosis, with no irregularity in size. The suspected lesion was localized to a limited area near the stomach wall. Although partial gastric adenocarcinoma was suspected, the cancers turned into gastric adenoma, atrophic gastritis, and enteroepithelium metaplastic carcinoma. Now, five years after the initial diagnosis, she maintains a good condition.

**CONCLUSIONS:** Laughter, one of our casual behaviors, has the effect of reducing the stress experienced by the human body. Laughter is expected to become alternative medicine in the future, and we hope to see more reports and evidence on soothing therapies using laughter.



We are grateful to the Prostate Cancer Foundation BC and the Canadian Breast Cancer Foundation (BC/Yukon) for their generous support of *Research Updates*.



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