



# RESEARCH UPDATES

For the latest in worldwide integrated cancer care

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**InspireHealth**  
INTEGRATED CANCER CARE

## In this issue

<b>Cancer</b>	<b>pg</b>
Breast	1
Colorectal	1
Prostate	2
Esophageal	3

<b>Therapies</b>	<b>pg</b>
Hormones	3
Vitamins	3
Supplements	4
Exercise	4

## CAM of the month pg 4

*Research Updates* is produced once a month by InspireHealth to inform those interested of newly published articles in integrative cancer care. Authoritative articles are selected based on their evidence and their relevance to this area of medicine.

Thank you to The Canadian Breast Cancer Foundation BC/Yukon Chapter for their generous support.



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## Breast

Warne AS. **Exploration of psychological and spiritual well-being of women with breast cancer participating in the art of living program.** *Diss Abstr Int. B. Sci Eng.* 2007;67(7):4122. The purpose of this study was to explore the psychological and spiritual well-being of women diagnosed with breast cancer who participated in a yoga-based stress-reduction program known as the Art of Living program. The mixed-method design involved the participation of 26 women, diagnosed with breast cancer within the past 5 years, in an 8-day yoga-based stress reduction course that includes yogic breathing techniques known as Sudarshan Kriya Yoga (SKY), as well as other processes that draw on yoga principles. Demographic and medical history variables were assessed at the time of recruitment, and standardized measures of quality of life, spiritual well-being, perceived stress, and positive states of mind were assessed two weeks prior to the beginning of the program, on the first day of the 8-day course, on the last day of the course, and following the 5-week maintenance period. In-depth semistructured interviews were conducted with a subsample of 12 women following the 5-week maintenance period. The results demonstrate a significant ( $p < 0.0001$ ) improvement in scores of all measurements after the 8-day Art of Living course and after the 5 weeks maintenance period. Effect sizes of all measurements were considered large. Results indicate that these effects were not due to maturation. Qualitative results demonstrated that the breast cancer experience was associated with distress and challenges, as well as growth and transformation. Qualitative themes indicated that the participation in the Art of Living program was associated with enhanced sense of spirituality, experiences of self-exploration, self-transcendence, and psychospiritual transformation. These pilot data represent a preliminary investigation of the relationship between mind-body-spirit, yoga-based practices, and psychospiritual well-being of women with breast cancer, highlighting the need for further controlled studies in this

area.\* \*This dissertation is a compound document (contains both a paper copy and a CD as part of the dissertation). The CD requires the following system requirements: Adobe Acrobat.

Cohen M, Fried G. **Comparing relaxation training and cognitive-behavioral group therapy for women with breast cancer.** *Res Soc Work Pract.* 2007;17(3):313-23. Objective: To assess the effectiveness of cognitive-behavior (CB) group intervention versus relaxation and guided imagery (RGI) group training. Method: A total of 114 early-stage breast cancer patients were randomly assigned to CB, RGI, or control groups, and instruments were completed at pre- and postintervention and 4 months later. Results: Psychological distress was significantly reduced in both intervention groups compared to the control group. The RGI group was more effective in reducing levels of fatigue and sleep difficulties, whereas the CB group was more effective in reducing external health locus of control. Internal health locus of control did not significantly change. Adherence to self-practice at home was significantly associated with reduction in psychological and physical symptoms. Conclusions: The study supports the use of both CB and RGI models for reducing psychological distress in breast cancer patients. RGI showed advantages in reducing fatigue and improving sleep quality, whereas CB better reduced external health locus of control perceptions

## Colorectal

Yang G, Shu X-O, Li H, et al. **Prospective cohort study of green tea consumption and colorectal cancer risk in women.** *Cancer Epidemiol Biomarkers Prev.* 2007;16(6):1219-1223. Tea and its constituents have shown anticarcinogenic activities in in vitro and animal studies. Epidemiologic studies, however, have been inconsistent. We prospectively evaluated the association between green tea consumption and colorectal cancer (CRC) risk in a cohort of 69,710 Chinese women aged 40 to 70 years.

Information on tea consumption was assessed through in-person interviews at baseline and reassessed 2 to 3 years later in a follow-up survey. During 6 years of follow-up, 256 incident cases of CRC were identified. The multivariate relative risk of CRC was 0.63 (95% confidence interval, 0.45-0.88) for women who reported drinking green tea regularly at baseline compared with nonregular tea drinkers. A significant dose-response relationship was found for both the amount of tea consumed (P trend = 0.01) and duration in years of lifetime tea consumption (P trend = 0.006). The reduction in risk was most evident among those who consistently reported to drink tea regularly at both the baseline and follow-up surveys (relative risk, 0.43; 95% confidence interval, 0.24-0.77). The inverse association with regular tea drinking was observed for both colon and rectal cancers. This study suggests that regular consumption of green tea may reduce CRC risk in women.

Meyerhardt JA, Niedzwiecki D, Hollis D, et al. **Association of dietary patterns with cancer recurrence and survival in patients with stage III colon cancer.** *JAMA.* 2007;298(7):754-764 Context Dietary factors have been associated with the risk of developing colon cancer but the influence of diet on patients with established disease is unknown. Objective To determine the association of dietary patterns with cancer recurrences and mortality of colon cancer survivors. Design, Setting, and Patients Prospective observational study of 1009 patients with stage III colon cancer who were enrolled in a randomized adjuvant chemotherapy trial (CALGB 89803) between April 1999 and May 2001. Patients reported on dietary intake using a semiquantitative food frequency questionnaire during and 6 months after adjuvant chemotherapy. We identified 2 major dietary patterns, prudent and Western, by factor analysis. The prudent pattern was characterized by high intakes of fruits and vegetables, poultry, and fish; the Western pattern was characterized by high intakes of meat, fat, refined grains, and dessert. Patients were followed up for cancer recurrence or death. Main Outcome Measures Disease-free survival, recurrence-free survival, and overall survival by dietary pattern. Results During a median follow-up of 5.3 years for the overall cohort, 324 patients had cancer recurrence, 223 patients died with cancer recurrence, and 28 died without documented cancer recurrence. A higher intake of a Western dietary pattern after cancer diagnosis was associated with a significantly worse disease-free survival (colon cancer recurrences or death). Compared with patients in the lowest quintile of Western dietary pattern, those in the highest quintile experienced an adjusted hazard ratio (AHR) for disease-free survival of 3.25 (95% confidence interval [CI], 2.04-5.19; P for trend  $\leq$ .001). The Western dietary pattern was associated with a similar detriment in recurrence free survival (AHR, 2.85; 95% CI, 1.75-4.63) and overall survival (AHR, 2.32; 95% CI, 1.36-3.96), comparing highest to lowest quintiles (both with P for trend  $\leq$ .001). The reduction in disease-free survival with a Western dietary pattern was not significantly modified by sex, age, nodal stage, body mass index, physical activity level, baseline performance status, or treatment group. In contrast, the prudent dietary pattern was not significantly associated with cancer recurrence or mortality. Conclusions Higher intake of a Western dietary pattern may be associated with a higher risk of recurrence and mortality among patients with stage III colon cancer treated with surgery and adjuvant chemotherapy. Further studies are needed to delineate which components of such a diet show the strongest association.

Theodoratou E, McNeill G, Cetnarskyj R, et al. **Dietary fatty acids and colorectal cancer: a case-control study.** *Am J*

*Epidemiol.* 2007;166(2):181-95. Fatty acid effects on colorectal cancer risk were examined in a national prospective case-control study in Scotland (1999-2006), including 1,455 incident cases and 1,455 matched controls. Three conditional logistic regression models adjusted for energy (residual method) and for other risk factors were applied in the whole sample and were stratified by sex, cancer site, age, and tumor staging. Total and trans-monounsaturated fatty acids and palmitic, stearic, and oleic acids were dose-dependently associated with colorectal cancer risk, but these effects did not persist after further energy adjustment. Significant dose-dependent reductions in risk were associated with increased consumption of omega-3 polyunsaturated fatty acids (highest vs. lowest quartile of intake: odds ratio = 0.63, 95% confidence interval: 0.50, 0.80; p < 0.0005 for trend) and of eicosapentaenoic (odds ratio = 0.59, 95% confidence interval: 0.47, 0.75; p < 0.0005 for trend) and docosahexaenoic (odds ratio = 0.63, 95% confidence interval: 0.50, 0.80; p < 0.0005 for trend) acids. These associations persisted after including energy with the nutrient-energy-adjusted term or total fatty acid intake (energy adjusted). The observed different effects of different types of fatty acids underline the importance of type of fat in the etiology and prevention of colorectal cancer.

## Prostate

Kirsh VA, Peters U, Mayne ST, et al. **Prospective study of fruit and vegetable intake and risk of prostate cancer.** *J Natl Cancer Inst.* 2007;99(15):1200-9. Background: Several epidemiologic studies have reported associations between fruit and vegetable intake and reduced risk of prostate cancer, but the findings are inconsistent and data on clinically relevant advanced prostate cancer are limited. Methods: We evaluated the association between prostate cancer risk and intake of fruits and vegetables in 1338 patients with prostate cancer among 29361 men (average follow-up = 4.2 years) in the screening arm of the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. Participants completed both a general risk factor and a 137-item food-frequency questionnaire at baseline. Cox proportional hazards models were used to estimate relative risks (RRs) and 95% confidence intervals (CIs). All statistical tests were two-sided. Results: Vegetable and fruit consumption was not related to prostate cancer risk overall; however, risk of extraprostatic prostate cancer (stage III or IV tumors) decreased with increasing vegetable intake (RR = 0.41, 95% CI = 0.22 to 0.74, for high versus low intake; P trend = .01). This association was mainly explained by intake of cruciferous vegetables (RR = 0.60, 95% CI = 0.36 to 0.98, for high versus low intake; P trend = .02), in particular, broccoli (RR = 0.55, 95% CI = 0.34 to 0.89, for >1 serving per week versus <1 serving per month; P trend = .02) and cauliflower (RR = 0.48, 95% CI = 0.25 to 0.89 for >1 serving per week versus <1 serving per month; P trend = .03). We found some evidence that risk of aggressive prostate cancer decreased with increasing spinach consumption, but the findings were not consistently statistically significant when restricted to extraprostatic disease. Conclusion: High intake of cruciferous vegetables, including broccoli and cauliflower, may be associated with reduced risk of aggressive prostate cancer, particularly extraprostatic disease.

 Thank you to the **BC Foundation for Prostate Disease** for their generous support.  
[www.BCPROSTATECANCER.org](http://www.BCPROSTATECANCER.org)

## Esophageal

Freedman ND, Park Y, Subar AF, et al. **Fruit and vegetable intake and esophageal cancer in a large prospective cohort study.** *Int J Cancer.* 2007 Aug 9; [Epub ahead of print]. Changing patterns of esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC) incidence worldwide suggest distinct etiologies. Although associations between fruit and vegetable intake and both ESCC and EAC have been found in multiple ecological and case-control studies, few prospective studies have investigated these associations. We prospectively examined these associations in 490,802 participants of the National Institutes of Health (NIH)-AARP Diet and Health Study using Cox models adjusted for age, alcohol intake, body mass index, cigarette smoking, education, physical activity and total energy intake. We present hazard ratios and 95% confidence intervals per serving per 1,000 calories. During 2,193,751 person years of follow-up, 103 participants were diagnosed with ESCC and 213 participants with EAC. We found a significant inverse association between total fruit and vegetable intake and ESCC risk (HR: 0.78, 95% CI: 0.67-0.91), but not EAC risk (0.98, 0.90-1.08). In models mutually adjusted for fruit and vegetable intake, the protective association with ESCC was stronger for fruits (0.73, 0.57-0.93) than for vegetables (0.84, 0.66-1.07). When we examined botanical subgroups, we observed significant protective associations for ESCC and intake of Rosacea (apples, peaches, nectarines, plums, pears and strawberries) and Rutaceae (citrus fruits). A significant inverse association between EAC and Chenopodiaceae (spinach) intake was observed. Results from our study suggest that the relation of fruit and vegetable intake and esophageal cancer risk may vary by histologic type.

## Hormones

Dopfel RP, Schulmeister K, Schernhammer ES. **Nutritional and lifestyle correlates of the cancer-protective hormone melatonin.** *Cancer Detect Prev.* 2007;31(2):140-8. Context: Despite growing support for melatonin as a promising agent for cancer treatment and possibly cancer prevention, few studies have elucidated factors that influence endogenous melatonin. This overview summarizes dietary and lifestyle factors that have been shown to affect circulating melatonin levels. Biological Mechanisms: To date, many animal studies and in vitro experiments have illustrated that melatonin possesses oncostatic activity. Mechanisms that are currently being studied include melatonin's activity as an indirect antioxidant and free radical scavenger; its action on the immune system; suppression of fatty acid uptake and metabolism; and its ability to increase the degradation of calmoduline and to induce apoptosis. Studies further suggest that melatonin reduces local estrogen synthesis, through down-regulation of the hypothalamic-pituitary reproductive axis and direct actions of melatonin at the tumor cell level, thus behaving as a SERM. Therapeutic applications: Several small clinical trials have demonstrated that melatonin has some potential, either alone or in combination with standard cancer therapy, to yield favorable responses. Melatonin or its precursor tryptophan have been found in numerous edible plants, but more studies are needed to evaluate the influence of diets rich in tryptophan and melatonin on circulating melatonin levels in humans. Age, BMI, parity, and the use of certain drugs remain the factors that have been associated most consistently with aMT6s levels. Discussion: Further insights into the effects of dietary and lifestyle factors that modulate circulating melatonin levels may provide the basis for novel interventions to exploit melatonin for the prevention and treatment of human diseases.

Kayumov L, Lowe A, Rahman SA, et al. **Prevention of melatonin suppression by nocturnal lighting: relevance to cancer.** *Eur J Cancer Prev.* 2007;16(4):357-362.

The decreased melatonin production in humans and animals caused by environmental lighting, especially short wavelength lighting (between 470 and 525 nm) has been shown to be associated with an increased risk of cancer. The purpose of this study was to investigate whether blocking light in this wavelength range under bright light may prevent the suppression of melatonin, which could help to prevent cancer. Optical filter lenses were designed, allowing selective exclusion of all wavelengths below 530 nm. Salivary melatonin levels were measured under dim light (<5 lux), bright light (800 lux) and filtered light (800 lux) at hourly intervals between 2000 and 0800 h in 11 healthy young male participants (mean age 23.5+/-1.5 years). The measurements were taken during three nonconsecutive nights over a 2-week period. The Dim Light Melatonin Onset test was used as a marker of circadian phase. Nine of the 11 participants demonstrated preserved melatonin levels in filtered light similar to their dim light secretion profile. With filtered light, the participants had a mean relative amount of melatonin of 91.2 (P>0.05 between dim light and experimental condition). Unfiltered bright light drastically suppressed melatonin production with a mean relative amount of melatonin of 25.4 (P<0.05 between dim light and experimental condition). Preventing melatonin deficiencies using lenses that block light of low wavelength from reaching the retina presents a cost-effective, practical solution to the problem of increased malignancy rates in shift workers.

## Vitamins

Wu K, Feskanich D, Fuchs CS, et al. **A nested case control study of plasma 25-hydroxyvitamin D concentrations and risk of colorectal cancer.** *J Natl Cancer Inst.* 2007;99(14):1120-9.

Background: Low vitamin D status has long been implicated in colorectal carcinogenesis. We investigated this relationship in a nested case-control study within the Health Professionals Follow-up Study (HPFS), a large ongoing study of male health professionals living in the United States. Methods: Between 1993 and 2002, 179 colorectal cancer patients were diagnosed and matched to 356 control subjects by age and by month and year of blood collection. Results were also pooled with previously published results from the Nurses' Health Study (NHS) cohort, a large female cohort. Conditional logistic regression was used to analyze the association between plasma 25-hydroxyvitamin D [25(OH)D] and colorectal cancer, and pooled estimates were calculated using the method of DerSimonian and Laird. All statistical tests were two-sided. Results: In the HPFS, we observed a non-statistically significant inverse association between higher plasma 25(OH)D concentration and risk of colorectal cancer and a statistically significant inverse association for colon cancer (highest versus lowest quintile: odds ratio [OR] = 0.46, 95% confidence interval [CI] = 0.24 to 0.89; P(trend) = .005). After pooling the results from the HPFS and NHS, higher plasma 25(OH)D concentrations were statistically significantly associated with decreased risks of both colorectal cancer (highest versus lowest quintile, OR = 0.66, 95% CI = 0.42 to 1.05; P(trend) = .01) and colon cancer (highest versus lowest quintile, OR = 0.54, 95% CI = 0.34 to 0.86; P(trend) = .002). Inverse associations with plasma 25(OH)D concentration did not differ by location of colon cancer (proximal versus distal), but the number of patients was small and none of the associations was statistically significant. Opposite relationships between plasma 25(OH)D levels and risk of rectal cancers were found among men (positive) and women (inverse). Conclusion: Our

data provide additional support for the inverse association between vitamin D and colorectal and, in particular, colon cancer risk.

### Supplements

Walfisch S, Walfisch Y, Kirilov E, et al. **Tomato lycopene extract supplementation decreases insulin-like growth factor-I levels in colon cancer patients.** *Eur J Cancer Prev.* 2007;16(4):298-303.

Epidemiological studies have shown that high serum levels of insulin-like growth factor-I are associated with an increased risk of colon and other types of cancer. The aim of this study was to determine whether short intervention with dietary tomato lycopene extract will affect serum levels of the insulin-like growth factor system components in colon cancer patients. The study had a double-blind, randomized, placebo-controlled design. Colon cancer patients (n=56), candidates for colectomy, were recruited from the local community a few days to a few weeks before surgery. Personal and medical data were recorded. Plasma concentrations of insulin-like growth factor-I and II and insulin-like growth factor-I-binding protein-3 were assayed by routine laboratory methods. Lycopene was assayed by high-performance liquid chromatography. Plasma lycopene levels increased by twofold after supplementation with tomato lycopene extract. In the placebo-treated group, there was a small nonsignificant increase in lycopene plasma levels. The plasma concentration of insulin-like growth factor-I decreased significantly by about 25% after tomato lycopene extract supplementation as compared with the placebo-treated group (P<0.05). No significant change was observed in insulin-like growth factor-I-binding protein-3 or insulin-like growth factor-II, whereas the insulin-like growth factor-I/insulin-like growth factor-I-binding protein-3 molar ratio decreased significantly (P<0.05). Given that high plasma levels of insulin-like growth factor-I have been suggested as a risk factor for various types of cancer including colon cancer, the results support our suggestion that tomato lycopene extract has a role in the prevention of colon and possibly other types of cancer.

### Exercise

Carson JW, Carson KM, Porter LS, et al. **Yoga for women with metastatic breast cancer: results from a pilot study.** *J Pain Symptom Manage.* 2007;33(3): 331-341.

Metastatic breast cancer (MBC) remains a terminal illness for which major treatment advances are slow to appear, and hence it is crucial that effective palliative interventions be developed to reduce the cancer-related symptoms of women with this condition during the remaining years of their lives. This pilot/feasibility study examined a novel, yoga-based palliative intervention, the Yoga of Awareness Program, in a sample of women with MBC. The eight-week protocol included gentle yoga postures, breathing exercises, meditation, didactic presentations, and group interchange. Outcome was assessed using daily measures of pain, fatigue, distress, invigoration, acceptance, and relaxation during two preintervention weeks and the final two weeks of the intervention. Thirteen women completed the intervention (mean age = 59; mean time since diagnosis = 7 years; two African American, 11 Caucasian). During the study, four participants had cancer recurrences, and the physical condition of several others deteriorated noticeably. Despite low statistical power, pre-to-post multilevel outcomes analyses showed significant increases in invigoration and acceptance. Lagged analyses of length of home yoga practice (controlling for individual mean practice time and outcome levels on the lagged days) showed that on the day after a day during which women practiced more, they experienced

significantly lower levels of pain and fatigue, and higher levels of invigoration, acceptance, and relaxation. These findings support the need for further investigation of the effects of the Yoga of Awareness Program in women with MBC.

### CAM of the month

Mai Z. **Soy phytochemicals synergistically enhance the preventive effect of tamoxifen on the growth of estrogen-dependent human breast carcinoma in mice.** *Carcinogenesis.* 2007;28(6):1217-23.

The objective of this work was to determine the interactive effects between soy bioactive components and tamoxifen (TAM) on prevention of estrogen-dependent breast cancer (BRCA). We initially investigated the effects of soy isoflavone genistein and TAM on the growth and cell cycle progression of estrogen-dependent MCF-7 human BRCA cells, and on the expression of ERalpha, pS2 and EGFR genes in vitro. Genistein or TAM alone inhibited the growth of MCF-7 cells in part via G(1) phase arrest, but their combinations showed suggestive antagonistic effects. We further evaluated the effects of bioactive soy components and TAM on the growth inhibition of MCF-7 tumors in a clinically relevant breast tumor model. TAM and bioactive soy components, genistein and soy phytochemical concentrate (SPC), delayed the growth of MCF-7 tumors. The combination of TAM with genistein or SPC, especially at the lower dose of TAM, had synergistic effects on delaying the growth of MCF-7 tumors. Biomarker determination suggests that the combination of TAM and soy components may synergistically delay the growth of MCF-7 tumors via their combined effects on induction of tumor cell apoptosis and inhibition of tumor cell proliferation. In addition, genistein and TAM combination synergistically delayed the growth of breast tumor via decreased estrogen level and activity, and down-regulation of EGFR expression. The results from our studies suggest that further investigations may be warranted to determine if the combination of TAM and bioactive soy components may be used for prevention and/or treatment of estrogen-dependent BRCA.

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