



# RESEARCH UPDATES

For the latest in world-wide integrated cancer care research



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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.

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## Breast

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):331-41.

Major treatment advances are slow to appear for metastatic breast cancer (MBC), and hence it is crucial that effective palliative interventions be developed to reduce the cancer-related symptoms of women living with this condition. 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.

Nikander R, Sievanen H, Ojala K, et al. **Effect of a vigorous aerobic regimen on physical performance in breast cancer patients: A randomized controlled pilot trial.** *Acta Oncologica* 2007;46(2):181-6.

This randomized, controlled pilot trial was carried out to assess the feasibility and efficacy of an aerobic exercise in enhancing physical performance of breast cancer patients after adjuvant treatments. The potential of the training regimen to prevent accompanying bone loss

was also assessed. Thirty patients, 41-65 years of age, were randomly assigned into training or control groups shortly after adjuvant chemo- or radiotherapy. The 12-week training included a guided aerobic exercise session once a week (the effective part being either step aerobic- or circuit-training in alternate weeks) and similar home exercise sessions twice a week. Adherence to the guided sessions was 78%, while home training was performed an average 2.1 times per week. Agility assessed with figure-8 running test and peak jumping power showed significant between-group treatment-effects (~5% and ~10%, respectively). Judged from the accelerometer data, reaction forces up to six times body weight occurred during the training, which implies that the training could also have potential to affect bone mass. The present exercise regimen turned out to be feasible and effective among breast cancer patients in terms of physical performance. Large controlled trials are necessary to confirm these findings.

Ah DV. **Stress, optimism, and social support: impact on immune responses in breast cancer.** *Res Nursing Health* 2007;30(1):72-83

Abstract: The purpose of this study was to examine the direct and stress-buffering effect of optimism and satisfaction with social support on immune responses in women with breast cancer. Participants were 54 post-operative (M = 19 days) breast cancer patients who completed questionnaires on stress, optimism, and satisfaction with social support and provided blood to measure natural killer cell activity (NKCA) and interferon-gamma (IFN-[gamma]) from whole blood. Higher levels of stress were associated with decrements in NKCA and IFN-[gamma]. Optimism moderated the relationship of stress on NKCA but was not related to IFN-[gamma]. Satisfaction with social support was unrelated to immune responses. Results suggest that interventions aimed at reducing stress and enhancing optimism in women with breast cancer might promote optimal immune response.

Rebeck TR. **A retrospective case-control study of the use of hormone-related supplements and association with breast cancer.** *Int J Cancer* 2007;120 (7):1523-8.

Hormone-related supplements (HRS), many of which contain phytoestrogens, are widely used to manage menopausal symptoms, yet their relationship with breast cancer risk has generally not been evaluated. We evaluated whether use of HRS was associated with breast cancer risk, using

a population-based case-control study in 3 counties of the Philadelphia metropolitan area consisting of 949 breast cancer cases and 1,524 controls. Use of HRS varied significantly by race, with African American women being more likely than European American women to use any herbal preparation (19.2% vs. 14.7%,  $p=0.003$ ) as well as specific preparations including black cohosh (5.4% vs. 2.0%,  $p=0.003$ ), ginseng (12.5% vs. 7.9%,  $p<0.001$ ) and red clover (4.7% vs. 0.6%,  $p<0.001$ ). Use of black cohosh had a significant breast cancer protective effect (adjusted odds ratio 0.39, 95% CI: 0.22-0.70). This association was similar among women who reported use of either black cohosh or Remifemin (an herbal preparation derived from black cohosh; adjusted odds ratio 0.47, 95% CI: 0.27-0.82). The literature reports that black cohosh may be effective in treating menopausal symptoms, and has antiestrogenic, antiproliferative and antioxidant properties. Additional confirmatory studies are required to determine whether black cohosh could be used to prevent breast cancer.

Porojnicu AC, Lagunova Z, Robsahm TE, et al. **Changes in risk of death from breast cancer with season and latitude: sun exposure and breast cancer survival in Norway.** *Br Cancer Res Treat* 2007;102(3):323-8.

The Norwegian counties can conveniently be divided in three groups with different annual UV exposures and different incidence rates of squamous cell carcinoma (SCC) of the skin. In view of the hypothesis that latitude and season of diagnosis may play a role for breast cancer progression, the prognosis of breast cancer as determined for summer and winter diagnosis, were evaluated in the three residential regions. Two age groups were analysed separately (stratification at 50 years). For all regions, and for all ages, the prognosis was best for women diagnosed in the summer season (Relative risk (RR) of death was 15-25% lower for summer diagnosis versus winter diagnosis). There was no significant seasonal variation of the number of new cases. For women diagnosed before the age of 50, a geographical gradient in cancer prognosis was also found (RR of death 0.6, 95% CI: 0.5-0.7 for cases diagnosed in southeast Norway and RR of death 0.8, 95% CI: 0.6-1.1 for diagnosis in the north of Norway). This is in agreement with a 1.5 times larger annual UV exposures and 3-4 times larger incidence rates of SCC in the southeast region when compared with the north region. For women diagnosed after the age of 50, no significant difference was found between the three regions. Despite a 17% higher vitamin D intake from food in north of Norway no difference in cancer survival was found for diagnosis during winter (when no significant differences in the levels of UV exposure can be detected between regions). The overall data support our earlier hypothesis that season of diagnosis and therapy start improves the survival for breast cancer.

## Prostate

Kurahashi N, Iwasaki M, Sasazuki S, et al. **Soy product and isoflavone consumption in relation to prostate cancer in Japanese men.** *Cancer Epidemiol Biomarkers Prev* 2007;16(3):538-45.

The incidence of prostate cancer is much lower in Asian than Western populations. Environmental factors, such as dietary habits, may play a major role in the causation of prostate cancer. Although isoflavones have been suggested to show a preventive effect against prostate cancer in animal experiments, the results of epidemiologic studies are

inconsistent. Here, we conducted a population-based prospective study in 43,509 Japanese men ages 45 to 74 years who generally have a high intake of isoflavones and low incidence of prostate cancer. Participants responded to a validated questionnaire, which included 147 food items. During follow-up from 1995 through 2004, 307 men were newly diagnosed with prostate cancer, of which 74 cases were advanced, 220 cases were organ localized, and 13 cases were of an undetermined stage. Intakes of genistein, daidzein, miso soup, and soy food were not associated with total prostate cancer. However, these four items decreased the risk of localized prostate cancer. In contrast, positive associations were seen between isoflavones and advanced prostate cancer. These results were strengthened when analysis was confined to men ages >60 years, in whom isoflavones and soy food were associated with a dose-dependent decrease in the risk of localized cancer, with relative risks for men in the highest quartile of genistein, daidzein, and soy food consumption compared with the lowest of 0.52 [95% confidence interval (95% CI), 0.30-0.90], 0.50 (95% CI, 0.28-0.88), and 0.52 (95% CI, 0.29-0.90), respectively. In conclusion, we found that isoflavone intake was associated with a decreased risk of localized prostate cancer.

Gong Z, Agalliu I, Lin DW, Stanford JL. **Obesity is associated with increased risks of prostate cancer metastasis and death after initial cancer diagnosis in middle-aged men.** *J Clin Oncol* 2007;109(6):1192-202.

**BACKGROUND:** Current research is inconclusive regarding the effect of obesity on outcomes after a prostate cancer diagnosis. The objective of this study was to examine associations between obesity and the risks of developing metastasis or prostate cancer-specific mortality in a population-based cohort of men with prostate cancer. **METHODS:** Seven hundred fifty-two middle-aged men with prostate cancer who were enrolled in a case-control study and remain under long-term follow-up for disease progression and mortality formed the study cohort. Body mass index (BMI) in the year before diagnosis was obtained at the time of initial interview. Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (95% CIs) of prostate cancer metastasis and mortality associated with obesity, controlling for age, race, smoking status, Gleason score, stage at diagnosis, diagnostic prostate-specific antigen level, and primary treatment. **RESULTS:** Obesity (BMI  $\geq 30$  kg/m<sup>2</sup>) was associated with a significant increase in prostate cancer mortality (HR, 2.64; 95% CI, 1.18-5.92). Among men who were diagnosed with local- or regional-stage disease, obesity also was associated with an increased risk of developing metastasis (HR, 3.61; 95% CI, 1.73-7.51). Associations generally were consistent across strata defined by Gleason score (2-6 or 7 [3 + 4] vs 7 [4 + 3] or 8-10), stage (local vs regional/distant for mortality), and primary treatment (androgen-deprivation therapy use: yes vs no). **CONCLUSIONS:** Obesity at the time of diagnosis was associated with increased risks of prostate cancer metastasis and death. The increased risk of prostate cancer death or metastasis associated with obesity largely was independent of key clinical prognostic factors at diagnosis.

Tuohimaa P, Tenkanen L, Syvala H, et al. **Interaction of factors related to the metabolic syndrome and vitamin D on risk of prostate cancer.** *Cancer Epidemiol Biomarkers Prev* 2007;16(2):302-7.

**Background:** Factors related to the metabolic syndrome and low levels of vitamin D have been implicated as risk factors for

prostate cancer. Insofar, no studies have assessed their joint effects on prostate cancer risk. Methods: We studied (a) the associations of vitamin D with the metabolic syndrome factors body mass index, systolic and diastolic blood pressure, and high-density lipoprotein cholesterol (HDL-C) and (b) the prostate cancer risk associated with these factors and especially their joint effects with vitamin D on risk of prostate cancer. We did a longitudinal nested case-control study on 132 prostate cancer cases and 456 matched controls from a cohort of 18,939 Finnish middle-aged men from the Helsinki Heart Study. The odds ratios (OR) of prostate cancer were assessed via conditional logistic regression analysis. Results: Apart from HDL-C, there was no linear association between the metabolic syndrome factors and vitamin D levels. In univariate analysis, men in the highest quartiles of body mass index ( $>28$  kg/m<sup>2</sup>) and systolic blood pressure ( $>150$  mmHg) showed a modest increase in risks of prostate cancer, with ORs of 1.37 ( $P = 0.16$ ) and 1.53 ( $P = 0.05$ ) when compared with the three lower quartiles, but low HDL-C entailed no prostate cancer risk. However, with all three factors present, the OR was 3.36 ( $P = 0.02$ ), and jointly with low vitamin D ( $\leq 40$  nmol/L), the OR was 8.03 ( $P = 0.005$ ) compared with those with no metabolic syndrome factors and intermediate levels of vitamin D. There was an interaction between vitamin D and the metabolic syndrome factors so that a clustering of these factors entailed high risk of prostate cancer but only if vitamin D level was low ( $\leq 40$  nmol/L). If it was at intermediate levels, the metabolic syndrome factors entailed no prostate cancer risk. Conclusions: We conclude that the prostate cancer risk associated with factors related to the metabolic syndrome is strongly conditioned by levels of vitamin D.

BC Foundation for Prostate Disease



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## Colorectal

Park S-Y, Murphy SP, Wilkens LR, et al. **Calcium and vitamin D intake and risk of colorectal cancer: the multiethnic cohort study.** *Am J Epidemiol* 2007;165(7):784-93.

The associations of intakes of calcium and vitamin D with colorectal cancer risk were examined in the Multiethnic Cohort Study (Hawaii and Los Angeles, California). In 1993–1996, 85,903 men and 105,108 women aged  $\geq 45$  years completed a quantitative food frequency questionnaire. A total of 2,110 incident cases of colorectal cancer (1,138 in men and 972 in women) were identified through December 31, 2001. Cox proportional hazards models were used to calculate multivariate-adjusted relative risks and 95% confidence intervals. Total calcium intake (from foods and supplements) was inversely associated with colorectal cancer risk in both men (highest quintile vs. lowest: relative risk (RR) = 0.70, 95% confidence interval (CI): 0.52, 0.93;  $p$  for trend = 0.006) and women (RR = 0.64, 95% CI: 0.50, 0.83;  $p$  for trend = 0.003). The inverse association was also seen for total vitamin D intake in men (RR = 0.72, 95% CI: 0.51, 1.00;  $p$  for trend = 0.03) but not in women. Intake of dairy products was inversely associated with colorectal cancer risk, especially among nonusers of supplemental calcium (men: RR = 0.77, 95% CI: 0.59, 1.01; women: RR = 0.66, 95% CI: 0.49, 0.89). The findings support the hypothesis of protective roles for calcium, vitamin D, and dairy products in the risk of colorectal cancer.

## Ovarian

Beral V. **Ovarian cancer and hormone replacement therapy in the Million Women Study.** *Lancet* 2007. Pub online April 19, 2007.

Background: Ovarian cancer is the fourth most common cancer in women in the UK, with about 6700 developing the malignancy and 4600 dying from it every year. However, there is limited information about the risk of ovarian cancer associated with the use of hormone replacement therapy (HRT). Methods: 948,576 postmenopausal women from the UK Million Women Study who did not have previous cancer or bilateral oophorectomy were followed-up for an average of 53 years for incident ovarian cancer and 69 years for death. Information on HRT use was obtained at recruitment and updated where possible. Relative risks for ovarian cancer were calculated, stratified by age and hysterectomy status, and adjusted by area of residence, socioeconomic group, time since menopause, parity, body-mass index, alcohol consumption, and use of oral contraceptives. Findings: When they last reported HRT use, 287,143 women (30%) were current users and 186,751 (20%) were past users. During follow-up, 2273 incident ovarian cancers and 1591 deaths from the malignancy were recorded. Current users were significantly more likely to develop and die from ovarian cancer than never users (relative risk 1.20 [95% CI 1.09–1.32;  $p=0.0002$ ] for incident disease and 1.23 [1.09–1.38;  $p=0.0006$ ] for death). For current users of HRT, incidence of ovarian cancer increased with increasing duration of use, but did not differ significantly by type of preparation used, its constituents, or mode of administration. Risks associated with HRT varied significantly according to tumour histology ( $p<0.0001$ ), and in women with epithelial tumours the relative risk for current versus never use of HRT was greater for serous than for mucinous, endometrioid, or clear cell tumours (1.53 [1.31–1.79], 0.72 [0.52–1.00], 1.05 [0.77–1.43], or 0.77 [0.48–1.23], respectively). Past users of HRT were not at an increased risk of ovarian cancer (0.98 [0.88–1.11] and 0.97 [0.84–1.11], respectively, for incident and fatal disease). Over 5 years, the standardised incidence rates for ovarian cancer in current and never users of HRT were 2.6 (2.4–2.9) and 2.2 (2.1–2.3) per 1000, respectively—ie, one extra ovarian cancer in roughly 2500 users; death rates were 1.6 (1.4–1.8) and 1.3 (1.2–1.4) per 1000, respectively—ie, one extra ovarian cancer death in roughly 3300 users. Interpretation: Women who use HRT are at an increased risk of both incident and fatal ovarian cancer. Since 1991, use of HRT has resulted in some 1300 additional ovarian cancers and 1000 additional deaths from the malignancy in the UK.

## Prevention

Soerjomataram I, De Vries E, Pukkala E, Coebergh JW.

**Excess of cancers in Europe: A study of eleven major cancers amenable to lifestyle change.** *Int J Cancer* 2007;120(6):1336-43.

Worldwide an estimated 11 million cancer cases were diagnosed in 2002, one quarter being in Europe. We estimated the potential in avoidable numbers and proportions of 11 cancers amenable to prevention (cancers of the oral cavity, oesophagus, stomach, colorectal, pancreas, laryngeal, lung, female breast, endometrium, kidney and bladder) in 28 European countries. We assumed that the aggregated rate of 3 countries with lowest incidence to be attainable throughout Europe. The difference between the age- and gender-specific national cancer incidence rates and the lowest rate observed in

2002 was determined and defined as 'avoidable.' Of the 1.4 million adult cases of selected cancers and countries within our study, 363,000 (59%) cancers in males and 326,000 (45%) cancers in females were hypothetically avoidable. Among men, the proportion was largest in Hungary (77%) and among women, in Belgium (54%). Assuming that differences in cancer incidence are not attributable to genetic susceptibility or diagnostic activity, about 50% of all cases of these 11 cancers could be potentially avoided, especially by decreased smoking among men. Interventions directed at reducing smoking, obesity and alcohol use as well as increasing physical activity and fruit and vegetable intake are necessary to attain lower incidence rates. It is important to recognize that the actual preventable cancer by eliminating currently known risk factors is somewhat less than we have estimated.

## Supplements

Simone II CB, Simone NL, Simone V, Simone CB. **Antioxidants and other nutrients do not interfere with chemotherapy or radiation therapy and can increase kill and increase survival, part 2.**

*Alt Ther Health Med* 2007;13(2):40-7.

Purpose: Some in the oncology community contend that patients undergoing chemotherapy and/or radiation therapy should not use food supplement antioxidants and other nutrients. Oncologists at an influential oncology institution contended that antioxidants interfere with radiation and some chemotherapies because those modalities kill by generating free radicals that are neutralized by antioxidants, and that folic acid interferes with methotrexate. This is despite the common use of amifostine and dexrazoxane, 2 prescription antioxidants, during chemotherapy and/or radiation therapy. Design: To assess all evidence concerning antioxidant and other nutrients used concomitantly with chemotherapy and/or radiation therapy. The MEDLINE and CANCERLIT databases were searched from 1965 to November 2003 using the words vitamins, antioxidants, chemotherapy, and radiation therapy. Bibliographies of articles were searched. All studies reporting concomitant nutrient use with chemotherapy and/or radiation therapy (280 peer-reviewed articles including 62 in vitro and 218 in vivo) were indiscriminately included. Results: Fifty human clinical randomized or observational trials have been conducted, involving 8,521 patients using beta-carotene; vitamins A, C, and E; selenium; cysteine; B vitamins; vitamin D<inf>3</inf>; vitamin K<inf>3</inf>; and glutathione as single agents or in combination. Conclusions: Since the 1970s, 280 peer-reviewed in vitro and in vivo studies, including 50 human studies involving 8,521 patients, 5,081 of whom were given nutrients, have consistently shown that do not interfere with therapeutic modalities for cancer. Furthermore, non-prescription antioxidants and other nutrients enhance the killing of therapeutic modalities for cancer, decrease their side effects, and protect normal tissue. In 15 human studies, 3,738 patients who took non-prescription antioxidants and other nutrients actually had increased survival.

## Acupuncture

Johnston MF, Yang C, Hui K-K, et al. **Acupuncture for chemotherapy-associated cognitive dysfunction: A hypothesis-generating literature review to inform clinical advice.** *Int Cancer Ther* 2007;6(1):36-41.

There is an emerging consensus that between one fifth and one half of breast cancer patients experience chemotherapy-associated cognitive dysfunction. Research shows that

patients with cancer are often interested in acupuncture for symptom relief. A clinical question thus arises: What should physicians advise their patients regarding the use of acupuncture to alleviate or ameliorate chemotherapy-associated cognitive dysfunction? The authors review and synthesize 2 bodies of relevant research literature: (1) the developing literature on the etiology and nature of chemotherapy-associated cognitive dysfunction and (2) the literature concerning acupuncture for neurological diseases and psychological issues. There is evidence that acupuncture may be effectively used to manage a range of psychoneurological issues, some of which are similar to those experienced by patients with chemotherapy-associated cognitive dysfunction. The evidence of efficacy is more promising for psychological than neurological conditions. Given evidence of possible efficacy combined with evidence of demonstrated safety, we suggest that physicians should support patient decisions to use acupuncture services for chemotherapy-associated cognitive dysfunction, especially given the lack of proven alternatives.

## CAM of the Month

Yildirim S, Gurkan A. **The influence of music on anxiety and the side effects of chemotherapy.** *Anadolu Psikiyatri Dergisi* 2007;8(1):37-45.

Objective: This purpose of this research is to investigate the influence of music on anxiety level and the side effects on the acute patients undergoing chemotherapy. Methods: The research data is obtained by using Patient Identification Form, State-Trait Anxiety Inventory, Cancer Symptoms Inventory and Chemotherapy Side Effect Inventory on both sample (N=30) and control (N=30) groups. While, the cancer patients in the sample group had undergone the alternative therapy for three times, the control group was excluded. For the assessment of the research data, chi-square, ANOVA and correlation analysis were carried out. Result: The findings indicated that, music has a meaningful relation with respect to anxiety states of the sample group ( $p>0.05$ ), and had no such a relation for the side effects of chemotherapy ( $p<0.001$ ). Conclusion: The investigation showed that, the clinical use of music as an alternative therapy has positive results in the reduction of anxiety in the patients and it is recommended to include the music therapy to regular nursing practices.

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