



## RESEARCH UPDATES DECEMBER 2012

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### FOR THE LATEST IN WORLDWIDE INTEGRATIVE CANCER CARE

**IN THIS ISSUE:** Burton and colleagues concluded that smoking and exercise are modifiable lifestyle factors for PSA levels in men with localized prostate cancer. Marshall et al. found that prostate cancer patients under active surveillance may benefit from daily vitamin D supplementation. Zhang and colleagues concluded that soy food intake is associated with longer survival and lower incidence of recurrence of breast cancer. Nikander and associates found that vigorous aerobic exercise can help to maintain bone strength and improve physical performance in breast cancer survivors. Dhruva et al. concluded that yoga breathing improved quality of life of cancer patients undergoing chemotherapy. Feng et al. found that Chinese medicine and chemotherapy is a safe and effective treatment for advanced-stage non-small cell lung cancer. Abdulrhman and colleagues found that honey and olive oil helped patients with chemotherapy-induced mucositis. Attia and associates concluded that Ginkgo Biloba supplements improved quality of life and cognitive function of brain tumour survivors. Olver and Dutney found that intercessory prayer improved the spiritual well-being of cancer patients. Birocco and colleagues reported that Reiki can improve quality of life of cancer patients. In our study of the month, Nissim et al. found that a brief psychosocial intervention can be beneficial for advanced cancer patients near the end of their lives.

## PROSTATE CANCER

Burton, AJ, R. M. Martin, J. L. Donovan, et al.

### Associations of Lifestyle Factors and Anthropometric Measures with Repeat PSA Levels during Active Surveillance/Monitoring.

*Cancer Epidemiology Biomarkers and Prevention.* 2012 October 2012; 21(10): 1877-1885.

**BACKGROUND:** Assessment of prostate-specific antigen increase with time (PSA growth) is a fundamental component of active surveillance among men with localized prostate cancer. Factors that influence PSA growth, however, are unclear. We evaluated associations of anthropometric and lifestyle factors with age-related PSA growth. **METHODS:** Repeat PSA measures from 404 men, aged 50 to 69 years, with localized prostate cancer undergoing active monitoring were obtained. From log(PSA) measures, age-specific multilevel mixed effect linear models were developed to predict PSA at age 50 years and yearly increase in postdiagnosis PSA. Baseline anthropometric measures, alcohol consumption, occupational class, smoking status, and physical activity were added to the model as covariates. **RESULTS:** The median number of repeat PSAs was 13 (range, 2-40), and the mean duration of follow-up was 4.8 years (SD, 2.3). The basic model of age-related PSA growth in men with localized prostate cancer estimated a mean PSA at age 50 of 3.95 ng/mL [95% confidence interval (CI): 3.55 to 4.39] and a yearly increase of 8.50% (95% CI: 7.90% to 9.10%). PSA at age 50 years was 2.1% lower per unit increase in weighted exercise score (95% CI: -3.3 to -0.8), 5.3% lower per 5 cm increase in height (95% CI: -9.4 to -1.1), and 24.5% higher (95% CI: 4.0 to 49.1) in current smokers than never smokers. Similar associations with PSA growth were seen. **CONCLUSION:** Smoking and exercise are modifiable lifestyle factors that may be associated with PSA levels in men with localized prostate cancer undergoing active monitoring/surveillance. **IMPACT:** These factors may be useful in understanding etiology of progression.

**INSPIREHEALTH'S INTERPRETATION:** Smoking may increase PSA in men with localized prostate cancer, and exercise may help lower PSA in men with localized prostate cancer.

Marshall, DT, S. J. Savage, E. Garrett-Mayer, et al.

### Vitamin D3 Supplementation at 4000 International Units Per Day for One Year Results in a Decrease of Positive Cores at Repeat Biopsy in Subjects with Low-Risk Prostate Cancer Under Active Surveillance.

*Journal of Clinical Endocrinology & Metabolism*. 2012 Jul; 97: 2315-2324.

**CONTEXT:** We wanted to investigate vitamin D in low-risk prostate cancer. **OBJECTIVES:** The objective of the study was to determine whether vitamin D(3) supplementation at 4000 IU/d for 1 yr is safe and would result in a decrease in serum levels of prostate-specific antigen (PSA) or in the rate of progression. **DESIGN:** In this open-label clinical trial (Investigational New Drug 77,839), subjects were followed up until repeat biopsy. **SETTING:** All subjects were enrolled through the Medical University of South Carolina and the Ralph H. Johnson Veterans Affairs Medical Center, both in Charleston, SC. **PATIENTS AND OTHER PARTICIPANTS:** All subjects had a diagnosis of low-risk prostate cancer. Fifty-two subjects were enrolled in the study, 48 completed 1 yr of supplementation, and 44 could be analyzed for both safety and efficacy objectives. **INTERVENTION:** The intervention included vitamin D(3) soft gels (4000 IU). **MAIN OUTCOME MEASURES:** Adverse events were monitored throughout the study. PSA serum levels were measured at entry and every 2 months for 1 yr. Biopsy procedures were performed before enrollment (for eligibility) and after 1 yr of supplementation. **RESULTS:** No adverse events associated with vitamin D(3) supplementation were observed. No significant changes in PSA levels were observed. However, 24 of 44 subjects (55%) showed a decrease in the number of positive cores or decrease in Gleason score; five subjects (11%) showed no change; 15 subjects (34%) showed an increase in the number of positive cores or Gleason score. **CONCLUSION:** Patients with low-risk prostate cancer under active surveillance may benefit from vitamin D(3) supplementation at 4000 IU/d.

**INSPIREHEALTH'S INTERPRETATION:** 4000 IU/day of vitamin D may be beneficial for men under active surveillance for prostate cancer.

## BREAST CANCER

Zhang, YF, H. B. Kang, B. L. Li and R. M. Zhang.

### Positive Effects of Soy Isoflavone Food on Survival of Breast Cancer Patients in China.

*Asian Pacific Journal of Cancer Prevention: Apjcp*. 2012 132: 479-482.

**AIM:** Soy foods are the major source of isoflavones, which are believed to play important roles in genesis of breast cancer and its progression. We here conducted a prospective study to evaluate the association of soy isoflavone food consumption with breast cancer prognosis. **METHODS:** A prospective study was performed from January 2004 and January 2006 in China. Trained interviewers conducted face-to-face interviews using a structured questionnaire to collect information on dietary habits and potential confounding factors. The relative risk [hazard ratio (HR)] and 95% CI were calculated from the Cox regression model for all significant predictors from cancer diagnosis to the endpoint of the study (event). **RESULTS:** After a median follow up of 52.1 months (range, 9-60 months), a total of 79 breast cancer related deaths were recorded in our study, risk being inversely associated with a high intake of soy isoflavone. With an average intake of soy isoflavone above 17.3 mg/day, the mortality of breast cancer can be reduced by about 38-36%. We also found the decreased breast cancer death with high soy protein intake, with a HR (95% CI) of 0.71 (0.52-0.98). Stratified analysis with reference to the ER status, further demonstrated a better prognosis of ER positive breast cancer with a high intake of soy isoflavone (HR 0.59, 0.40-0.93). **CONCLUSION:** Our study shows the soy food intake is associated with longer survival and low recurrence among breast cancer patients. A cohort study with a larger sample size and long term follow-up is now needed.

**INSPIREHEALTH'S INTERPRETATION:** Soy foods might help prolong survival and prevent recurrence of breast cancer

Nikander, R, H. Sievanen, K. Ojala, et al.

### Effect of Exercise on Bone Structural Traits, Physical Performance and Body Composition in Breast Cancer Patients - A 12-Month RCT.

*Journal of Musculoskeletal Neuronal Interactions*. 2012 September 2012; 123: 127-135.

**BACKGROUND:** In this 12-month RCT, we examined whether aerobic impact exercise training (3x/week) could facilitate breast cancer survivors' recovery by enhancing their bone structural strength, physical performance and body composition. **METHODS:** After the adjuvant chemo- and/ or radiotherapy, 86 patients were randomly assigned into the training or control group. Structural bone traits were assessed with pQCT at the tibia and with DXA at the femoral neck.

Agility (figure-8 running), jump force and power (force platform), grip strength and cardiovascular fitness (2-km walk test) were also assessed. Training effects on outcome variables were estimated by two-way factorial ANCOVA using the study group and menopausal status as fixed factors. **RESULTS:** Bone structural strength was better maintained among the trainees. At the femoral neck, there was a small but significant 2% training effect in the bone mass distribution ( $p=0.05$ ). At the tibial diaphysis, slight 1% to 2% training effects ( $p=0.03$ ) in total cross-sectional area and bone structural strength were observed ( $p=0.03$ ) among the postmenopausal trainees. Also, 3% to 4% training effects were observed in the figure-8 running time ( $p=0.03$ ) and grip strength ( $p=0.01$ ). **CONCLUSION:** In conclusion, vigorous aerobic impact exercise training has potential to maintain bone structural strength and improve physical performance among breast cancer survivors.

**INSPIREHEALTH'S INTERPRETATION:** Vigorous aerobic exercise can help maintain bone structure and improve physical condition in breast cancer survivors.

## YOGA BREATHING

Dhruva, A, C. Miaskowski, D. Abrams, et al.

### Yoga Breathing for Cancer Chemotherapy-Associated Symptoms and Quality of Life: Results of a Pilot Randomized Controlled Trial.

*Journal of Alternative & Complementary Medicine.* 2012 May; 185: 473-479.

**BACKGROUND:** Many debilitating symptoms arise from cancer and its treatment that are often unrelieved by established methods. Pranayama, a series of yogic breathing techniques, may improve cancer-related symptoms and quality of life, but it has not been studied for this purpose. **OBJECTIVES:** A pilot study was performed to evaluate feasibility and to test the effects of pranayama on cancer-associated symptoms and quality of life. **DESIGN:** This was a randomized controlled clinical trial comparing pranayama to usual care. **SETTING:** The study was conducted at a university medical center. **SUBJECTS:** Patients receiving cancer chemotherapy were randomized to receive pranayama immediately or after a waiting period (control group). **INTERVENTIONS:** The pranayama intervention consisted of four breathing techniques taught in weekly classes and practiced at home. The treatment group received pranayama during two consecutive cycles of chemotherapy. The control group received usual care during their first cycle, and received pranayama during their second cycle of chemotherapy. **OUTCOME MEASURES:** Feasibility, cancer-associated symptoms (fatigue, sleep disturbance, anxiety, depression, stress), and quality of life were the outcomes. **RESULTS:** Class attendance was nearly 100% in both groups. Sixteen (16) participants were included in the final intent-to-treat analyses. The repeated-measures analyses demonstrated that any increase in pranayama dose, with dose measured in the number of hours practiced in class or at home, resulted in improved symptom and quality-of-life scores. Several of these associations--sleep disturbance ( $p=0.04$ ), anxiety ( $p=0.04$ ), and mental quality of life ( $p=0.05$ )--reached or approached statistical significance. **CONCLUSIONS:** Yoga breathing was a feasible intervention among patients with cancer receiving chemotherapy. Pranayama may improve sleep disturbance, anxiety, and mental quality of life. A dose-response relationship was found between pranayama use and improvements in chemotherapy-associated symptoms and quality of life. These findings need to be confirmed in a larger study.

**INSPIREHEALTH'S INTERPRETATION:** Yoga breathing can help cancer patients undergoing chemotherapy.

## CHINESE MEDICINE

Feng, Y, Y. -Y Xiao, S. -D Li, et al.

### The Treatment of Non-Small Cell Lung Cancer by Interstitial I-125 Seeds Implantation Combined with Chemotherapy and Chinese Medicine.

*Chinese Journal of Integrative Medicine.* 2012 September 2012; 189: 663-669.

**OBJECTIVE:** To investigate the effects of brachytherapy with computed tomography-guided percutaneous radioactive I-125 seeds interstitial implantation (ISI) synchronized chemotherapy and Chinese medicine (CM) for the treatment of advanced stage of non-small cell lung cancer (NSCLC). **METHODS:** Ninety patients diagnosed with NSCLC by biopsy were randomly assigned to three groups: the synchronized therapy group (A), the chemotherapy plus CM-treated group (B), and the chemotherapy-treated group (C); a 2-month course of treatment was administered to them all. The effectiveness of treatment was evaluated based on tumor size, tumor markers (carcinoembryonic, squamous cell carcinoma-associated antigen, and cytokeratin 19 fragment), clinical symptoms, and quality of life (QOL) in patients. **RESULTS:** The total effective rates of Groups A to C were 83.33%, 46.67%, and 43.33%, respectively. The tumor markers were reduced obviously in Group A, showing significant difference compared with those in the other two groups. Additionally, QOL was

elevated and cancer-related symptoms were alleviated more significant[ly] in Group A than those in Group C (all  $P < 0.05$ ). **CONCLUSION:** The synchronized therapy of I-125 implantation with chemotherapy and CM was a safe therapeutic method and can be regarded as a new mode for treatment of advanced-stage NSCLC.

**INSPIREHEALTH'S INTERPRETATION:** Chinese medicine and chemotherapy can help patients with advanced-stage non-small cell lung cancer.

## HONEY

Abdulrhman, M, N. S. El Barbary, D. Ahmed Amin and R. Saeid Ebrahim.

### Honey and a Mixture of Honey, Beeswax, and Olive Oil-Propolis Extract in Treatment of Chemotherapy-Induced Oral Mucositis: A Randomized Controlled Pilot Study.

*Pediatric Hematology & Oncology. 2012 Apr; 293: 285-292.*

**BACKGROUND:** In spite of being one of the most investigated subjects among supportive care in cancer, no therapy has been found effective in treatment of chemotherapy-induced oral mucositis. **METHODS:** Based on the observations that honey bees products have anti-inflammatory and wound healing effects, the present study tried to evaluate the effect of topical application of honey and a mixture of honey, olive oil-propolis extract, and beeswax (HOPE) in treatment of oral mucositis. This was a randomized controlled clinical trial conducted on 90 patients with acute lymphoblastic leukemia and oral mucositis grades 2 and 3. The mean age of enrolled patients was 6.9 years. The patients were assigned into 3 equal treatment groups: Honey, HOPE, and control groups. Topical treatment for each patient consists of honey, HOPE, and benzocaine gel for honey, HOPE, and control groups, respectively. **RESULTS:** Recovery time in grade 2 mucositis was significantly reduced in the honey group as compared with either HOPE or controls ( $P < .05$ ). In grade 3 mucositis, recovery time did not differ significantly between honey and HOPE ( $P = 0.61$ ) but compared with controls, healing was faster with either honey or HOPE ( $P < .01$ ). Generally, in both grades of mucositis, honey produced faster healing than either HOPE or controls ( $P < .05$ ). **CONCLUSION:** Based on our results that showed that honey produced faster healing in patients with grade 2/3 chemotherapy-induced mucositis, we recommend using honey and possibly other bee products and olive oil in future therapeutic trials targeting chemotherapy-induced mucositis.

**INSPIREHEALTH'S INTERPRETATION:** Honey can help to reduce oral mucositis in patients undergoing chemotherapy.

## GINKGO BILOBA

Attia, A, S. R. Rapp, L. D. Case, et al.

### Phase II Study of Ginkgo Biloba in Irradiated Brain Tumor Patients: Effect on Cognitive Function, Quality of Life, and Mood.

*J Neurooncol. 2012 September 2012; 1092: 357-363.*

**BACKGROUND:** Ginkgo biloba has been reported to improve cognitive function in older adults and patients with Alzheimer's disease and multi-infarct dementia. **METHODS:** We conducted an open-label phase II study of this botanical product in symptomatic irradiated brain tumor survivors. Eligibility criteria included: life expectancy  $\geq 30$  weeks, partial or whole brain radiation  $\geq 6$  months before enrollment, no imaging evidence of tumor progression in previous 3 months, or stable or decreasing steroid dose, and no brain tumor treatment planned while on study. The Ginkgo biloba dose was 120 mg/day (40 mg t.i.d.) for 24 weeks followed by a 6-week washout period. Assessments performed at baseline, 12, 24 (end of treatment), and 30 weeks (end of washout) included KPS, Functional Assessment of Cancer Therapy-Brain (FACT-Br), Profile of Mood States, Mini-Mental Status Exam, Trail Making Test Parts A (TMT-A) and B (TMT-B), Digit Span Test, Modified Rey Osterrieth Complex Figure (ROCF), California Verbal Learning Test Part II, and the F-A-S Test. **RESULTS:** Of the 34 patients enrolled on study, 23 (68 %) completed 12 weeks of treatment and 19 (56 %) completed 24 weeks of treatment. There were significant improvements at 24 weeks in: executive function (TMT-B) ( $p = 0.007$ ), attention/concentration (TMT-A) ( $p = 0.002$ ), and non-verbal memory (ROCF-immediate/delayed recall) ( $p = 0.001/0.002$ ), mood ( $p = 0.002$ ), FACT-Br subscale ( $p = 0.001$ ), and the FACT physical subscale ( $p = 0.003$ ). **CONCLUSIONS:** Some improvement in quality of life and cognitive function were noted with Ginkgo biloba. However, treatment with Ginkgo biloba was associated with a high dropout rate.

**INSPIREHEALTH'S INTERPRETATION:** Ginkgo Biloba supplements can improve the quality of life and cognitive function of survivors of brain tumour.

## PRAYER

Olver, IN and A. Dutney.

### A Randomized, Blinded Study of the Impact of Intercessory Prayer on Spiritual Well-being in Patients with Cancer.

*Alternative Therapies in Health & Medicine.* 2012 Sep-Oct; 185: 18-27.

**CONTEXT:** Cochrane reviews have analyzed multiple studies on intercessory prayer that treatment teams had added to health interventions; however, the reviewers could draw no conclusions about the efficacy of prayer because the studies showed either positive or no effects and used different endpoints and methodologies. **OBJECTIVE:** The study intended to determine whether researchers could measure the impact of intercessory prayer on spiritual well-being. **DESIGN:** The research team conducted a randomized blinded trial of intercessory prayer added to normal cancer treatment with participants agreeing to complete quality of life (QOL) and spiritual well-being scales at baseline and 6 months later. The research team had shown previously that spiritual well-being is an important, unique domain in the assessment of QOL. Participants remained blinded to the randomization. Based on a previous study, the research team determined that the study required a sample of 1000 participants to detect small differences ( $P = .05$ , 2-tailed, 80% power). **SETTING:** The research team performed this research at the Royal Adelaide Hospital Cancer Centre, South Australia, Australia. **PARTICIPANTS:** Participants were patients at the cancer center between June 2003 and May 2008. Of 999 participants with mixed diagnoses who completed the baseline questionnaires, 66.6% provided follow-up. The average age was 61 years, and most participants were married/de facto (living with partners), were Australians or New Zealanders living in Australia, and were Christian. **INTERVENTION:** The research team asked an external group offering Christian intercessory prayer to add the study's participants to their usual prayer lists. They received details about the participants, but this information was not sufficient to identify them. **OUTCOME MEASURES:** The research team used the Functional Assessment of Chronic Illness Therapy-Spiritual Well-being questionnaire to assess spiritual wellbeing and QOL. **RESULTS:** The intervention group showed significantly greater improvements over time for the primary endpoint of spiritual well-being as compared to the control group ( $P = .03$ , partial  $\eta^2 = .01$ ). The study found a similar result for emotional well-being ( $P = .04$ , partial  $\eta^2 = .01$ ) and functional well-being ( $P = .06$ , partial  $\eta^2 = .01$ ). **CONCLUSIONS:** Participants with cancer whom the research team randomly allocated to the experimental group to receive remote intercessory prayer showed small but significant improvements in spiritual well-being.

**INSPIREHEALTH'S INTERPRETATION:** Intercessory prayer can improve the spiritual well-being of cancer patients.

## REIKI

Birocco, N, C. Guillame, S. Storto, et al.

### The Effects of Reiki Therapy on Pain and Anxiety in Patients Attending a Day Oncology and Infusion Services Unit.

*American Journal of Hospice & Palliative Medicine.* 2012 Jun; 294: 290-294.

**BACKGROUND:** Reiki is a system of natural healing techniques administered by laying of hands and transferring energy from the Reiki practitioner to the recipient. **METHODS:** We investigated the role of Reiki in the management of anxiety, pain and global wellness in cancer patients. Building on the results of a pilot project conducted between 2003 and 2005 by a volunteer association at our hospital, a wider, 3-year study was conducted at the same center. The volunteer Reiki practitioners received 2 years of theory and practical training. The study population was 118 patients (67 women and 51 men; mean age, 55 years) with cancer at any stage and receiving any kind of chemotherapy. Before each session, the nurses collected the patient's personal data and clinical history. Pain and anxiety were evaluated according to a numeric rating scale by the Reiki practitioners. Each session lasted about 30 min; pain and anxiety scores were recorded using a Visual Analog Scale (VAS), together with a description of the physical feelings the patients perceived during the session. All 118 patients received at least 1 Reiki treatment (total number, 238). **RESULTS:** In the subgroup of 22 patients who underwent the full cycle of 4 treatments, the mean VAS anxiety score decreased from 6.77 to 2.28 ( $P < .000001$ ) and the mean VAS pain score from 4.4 to 2.32 ( $P = .091$ ). Overall, the sessions were felt helpful in improving well-being, relaxation, pain relief, sleep quality and reducing anxiety. **CONCLUSION:** Offering Reiki therapy in hospitals could respond to patients' physical and emotional needs.

**INSPIREHEALTH'S INTERPRETATION:** Reiki can be beneficial for cancer patients.

## STUDY OF THE MONTH

Nissim, R, E. Freeman, C. Lo, et al.

### Managing Cancer and Living Meaningfully (CALM): A Qualitative Study of a Brief Individual Psychotherapy for Individuals with Advanced Cancer.

*Palliat Med.* 2012 Jul; 265: 713-721.

**BACKGROUND:** Although psychosocial care has been regarded as central to palliative and supportive care, there have been few empirically tested approaches to individual intervention. **AIM:** The subjective experience of advanced cancer patients receiving a new manualized brief individual psychotherapy, referred to as Managing Cancer and Living Meaningfully (CALM), was examined prior to the initiation of a randomized controlled trial testing the effectiveness of this intervention. **DESIGN:** Semi-structured interviews were conducted with patients who had a diagnosis of advanced cancer, and who underwent the intervention. **SETTING/PARTICIPANTS:** Patients were recruited from a large urban regional cancer center in Toronto, Canada. The 10 interviewees included seven women and three men. All had completed between three to six CALM sessions prior to the interview. **RESULTS:** The CALM intervention was associated with profound and unique patient-identified benefits and no patient-identified risks or concerns. Five interrelated benefits of the intervention were identified: (1) a safe place to process the experience of advanced cancer; (2) permission to talk about death and dying; (3) assistance in managing the illness and navigating the healthcare system; (4) resolution of relational strain; and (5) an opportunity to 'be seen as a whole person' within the healthcare system. These benefits were regarded by participants as unique in their cancer journey. **CONCLUSIONS:** Findings from a qualitative study suggest that the CALM intervention provides substantial benefits for patients with advanced cancer prior to the end of life. Findings informed the development of a randomized controlled trial to evaluate the effectiveness of this intervention.

**INSPIREHEALTH'S INTERPRETATION:** Psychotherapy can be beneficial for advanced cancer patients near the end of their lives.

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