



March 2010



InspireHealth
INTEGRATED CANCER CARE

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In this Issue

This month's edition of InspireHealth's Research Updates focuses on nutrition and stress management.

For example, Hughes et al. (p.2) report that dietary restriction during childhood reduces the risk of colon cancer and the *Study of the Month* by Kang et al. found that visceral obesity is an independent risk factor of colorectal cancer, and that insulin resistance was associated with the presence of colorectal cancer.

Foley et al. report that after training in mindfulness-based cognitive therapy, cancer patients experienced significant improvements in mindfulness, anxiety, depression, and quality of life.

InspireHealth Research Updates Focus Group

InspireHealth seeks to ensure that Research Updates are informative and user-friendly for our readers. To help us in this endeavour, we invite readers to participate in a focus group at InspireHealth on Monday, March 29 2010 from 2:00-3:30pm. If you are open to sharing your thoughts and feedback on this newsletter and are available to attend, please RSVP by email to Jan Rennie at rennie@inspirehealth.ca.

InspireHealth Research

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Research Updates is InspireHealth's monthly publication that informs those interested about authoritative articles in integrated cancer care. Articles are selected based on their evidence and relevance to integrated cancer care.

InspireHealth's 'Life Program', facilitated by our medical doctors, is an important opportunity to learn more about improving health and survival with a Cancer diagnosis. **Call today to register: 604 734 7125**

Breast Cancer

Beatty, L, C. Lee and T. D. Wade. **A Prospective Examination of Perceived Stress as a Mediator of the Relationship between Life-Events and QOL Following Breast Cancer.** *British Journal of Health Psychology.* 2009 November; 144: 789-804.

Objectives: This study prospectively investigated the relationship between life-events, perceived stress, and quality of life (QOL) following breast cancer diagnosis, using the bio-behavioural model of cancer stress as a framework. **Design.** A longitudinal, self-report design was used. **Methods.** Three waves of data from 10,543 mid-aged Australian women (aged 45-50 at Survey 1) were collected over 5 years as part of a population-based survey. From this group a subsample (N = 140) were identified who did not have breast cancer at Survey 1, but who subsequently developed breast cancer. Random regression growth curve analyses were used to investigate

whether perceived stress mediated the relationship between initial life-events and change in QOL functioning over time. Results. Prospective evidence was generated for each of the three criteria for testing mediation. As the number of life-events before breast cancer increased, women were significantly more likely to experience corresponding increases in perceived stress over the 5-year period. As the level of perceived stress before breast cancer increased, women were more likely to experience deteriorations over time in role emotional, role physical, vitality, bodily pain, physical functioning, and social functioning. As the number of life-events before breast cancer increased, women were at significant risk of experiencing deteriorations over time in bodily pain, social functioning, role emotional, and vitality. Mediation analyses revealed that perceived stress fully mediated the relationship between initial life-events and two QOL domains; role-emotional and social functioning. **Conclusion.**

Results partially supported the bio-behavioural model of cancer stress, but the model does not appear to fit the data as well as predicted, and may require revision.

Dai, Q, X. -O Shu, H. Li, et al. **Is Green Tea Drinking Associated with a Later Onset of Breast Cancer?**. *Ann Epidemiol.* 2010 January; 201: 74-81.

Background: Studies have found that tea polyphenols inhibit aromatase. Because of the substantial difference in levels of estrogens between premenopausal and postmenopausal women, the relationship between tea consumption and breast cancer risk may depend on menopausal status. **Methods:** We examined this hypothesis in the Shanghai Women's Health Study, a population-based cohort study of 74,942 Chinese women. **Results:** We found a time-dependent interaction between green tea consumption and age of breast cancer onset (p for interaction, 0.03). In comparison with non-tea drinkers, women who started tea-drinking at 25 years of age or younger had a hazard ratio (HR) of 0.69 (95% confidence interval [CI]: 0.41-1.17) to develop premenopausal breast cancer. On the other hand, compared with non-tea drinkers, women who started tea drinking at 25 years of age or younger had an increased risk of postmenopausal breast cancer with an HR of 1.61 (95% CI: 1.18-2.20). Additional analyses suggest regularly drinking green tea may delay the onset of breast cancer. **Conclusions:** Further studies are needed to confirm our findings.

Colorectal Cancer

Hughes, LAE, P. A. van den Brandt, A. P. de Bruine, et al. **Early Life Exposure to Famine and Colorectal Cancer Risk: A Role for Epigenetic Mechanisms.** *PLoS ONE.* 2009 411: Arte Number: e7951. ate of Pubaton: 23 No 2009.

Background: Exposure to energy restriction during childhood and adolescence is associated with a lower risk of developing colorectal cancer (CRC). Epigenetic dysregulation during this critical period of growth and development may be a mechanism to explain such observations. Within the Netherlands Cohort Study on diet and cancer, we investigated the association between early life energy restriction and risk of subsequent CRC characterized by the (promoter) CpG island methylation phenotype (CIMP). **Methodology/Principal Findings:** Information on diet and risk factors was collected by baseline questionnaire (n = 120,856). Three indicators of exposure were assessed: place of residence during the Hunger Winter (1944-45) and World War II years (1940-44), and father's employment status during the Economic Depression (1932-40). Methylation specific PCR (MSP) on DNA from paraffin embedded tumor tissue was performed to determine CIMP status according to the Weisenberger markers. After 7.3 years of follow-up, 603 cases and 4631 sub-cohort members were available for analysis. Cox regression was used to calculate hazard ratios (HR) and 95% confidence intervals for CIMP+ (27.7%) and CIMP- (72.3%) tumors according to the three time periods of energy restriction, adjusted for age and gender. Individuals exposed to severe famine during the Hunger Winter had a decreased risk of developing a tumor characterized by CIMP compared to those not exposed (HR

0.65, 95%CI: 0.45-0.92). Further categorizing individuals by an index of '0-1' '2-3' or '4-7' genes methylated in the promoter region suggested that exposure to the Hunger Winter was associated with the degree of promoter hypermethylation ('0-1 genes methylated' HR = 1.01, 95%CI:0.74-1.37; '2-3 genes methylated' HR = 0.83, 95% CI:0.61-1.15; '4-7 genes methylated' HR = 0.72, 95% CI:0.49-1.04). No associations were observed with respect to the Economic Depression and WWII years. **Conclusions:** This is the first study indicating that exposure to a severe, transient environmental condition during adolescence and young adulthood may result in persistent epigenetic changes that later influence CRC development.

Nutrition

Ahn, J, U. Lim, S. J. Weinstein, et al. **Prediagnostic Total and High-Density Lipoprotein Cholesterol and Risk of Cancer.** *Cancer Epidemiology, Biomarkers & Prevention.* 2009 Nov; 1811: 2814-2821.

BACKGROUND: Circulating total cholesterol has been inversely associated with cancer risk; however, the role of reverse causation and the associations for high-density lipoprotein (HDL) cholesterol have not been fully characterized. We examined the relationship between serum total and HDL cholesterol and risk of overall and site-specific cancers among 29,093 men in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study cohort. **METHODS:** Fasting serum total and HDL cholesterol were assayed at baseline, and 7,545 incident cancers were identified during up to 18 years of follow-up. Multivariable proportional hazards models were conducted to estimate relative risks (RR). **RESULTS:** Higher serum total cholesterol concentration was associated with decreased risk of cancer overall (RR for comparing high versus low quintile, 0.85; 95% confidence interval, 0.79-0.91; P trend 276.7 versus 55.3 versus <36.2 mg/dL). The inverse association of HDL cholesterol was evident for cancers of lung, prostate, liver, and the hematopoietic system, and the associations of HDL cholesterol with liver and lung cancers remained after excluding cases diagnosed within 12 years of study entry. **CONCLUSION:** Our findings suggest that prior observations regarding serum total cholesterol and cancer are largely explained by reverse causation. Although chance and reverse causation may explain some of the inverse HDL associations, we cannot rule out some etiologic role for this lipid fraction.

Dziaman, T, T. Huzarski, D. Gackowski, et al. **Selenium Supplementation Reduced Oxidative DNA Damage in Adnexectomized BRCA1 Mutations Carriers.** *Cancer Epidemiology, Biomarkers & Prevention.* 2009 Nov; 1811: 2923-2928.

Some experimental evidence suggests that BRCA1 plays a role in repair of oxidative DNA damage. Selenium has anticancer properties that are linked with protection against oxidative stress. To assess whether supplementation of BRCA1 mutation carriers with selenium have a beneficial effect concerning oxidative stress/DNA damage in the present double-blinded placebo control study, we determined 8-oxodG level in cellular DNA and urinary excretion of 8-oxodG and 8-oxoGua in the mutation carriers. We found that 8-oxodG level in leukocytes DNA is significantly higher in BRCA1 mutation

carriers. In the distinct subpopulation of BRCA1 mutation carriers without symptoms of cancer who underwent adnexectomy and were supplemented with selenium, the level of 8-oxodG in DNA decreased significantly in comparison with the subgroup without supplementation. Simultaneously in the same group, an increase of urinary 8-oxoGua, the product of base excision repair (hOGG1 glycosylase), was observed. Therefore, it is likely that the selenium supplementation of the patients is responsible for the increase of BER enzymes activities, which in turn may result in reduction of oxidative DNA damage. Importantly, in a double-blinded placebo control prospective study, it was shown that in the same patient groups, reduction in cancer incidents was observed. Altogether, these results suggest that BRCA1 deficiency contributes to 8-oxodG accumulation in cellular DNA, which in turn may be a factor responsible for cancer development in women with mutations, and that the risk to developed breast cancer in BRCA1 mutation carriers may be reduced in selenium-supplemented patients who underwent adnexectomy.

Myung SK. Ju W. Choi HJ. Kim SC. Korean Meta-Analysis (KORMA) Study Group **Soy Intake and Risk of Endocrine-Related Gynaecological Cancer: A Meta-Analysis** *BJOG: An International Journal of Obstetrics & Gynaecology*. 2009 Dec; 11613: 1697-1705.

BACKGROUND: Epidemiology studies have reported associations between soy intake and the risk of endocrine-related gynaecological cancers. However, to date there have been no quantitative meta-analyses reported regarding this topic. **OBJECTIVES:** We investigated the quantitative associations between soy food intake and the risk of endometrial cancer and ovarian cancer by a meta-analysis of case-control studies and cohort studies. **SEARCH STRATEGY:** We searched MEDLINE (PubMed), EMBASE and the Cochrane Library during October 2008 using common keywords related to soy intake and endometrial or ovarian cancer. Two evaluators independently reviewed and selected articles, based on predetermined selection criteria. **SELECTION CRITERIA:** Included studies met all of the following criteria: (1) a case-control study or cohort study (to date, no randomized controlled trials have been reported); (2) investigated the associations between 'soy or soy product intake' and 'endometrial cancer' or 'ovarian cancer'; (3) reported outcome measures with adjusted odds ratios (OR) or relative risks (RR) and 95% confidence intervals (CI). **DATA COLLECTION AND ANALYSIS:** We investigated the associations between the overall soy intake (highest versus lowest intake) and the risk of endocrine-related gynaecological cancers (endometrial or ovarian cancer) as the main analysis. We also performed subgroup analyses by type of cancer (endometrial or ovarian), type of study design (case-control or cohort) and type of soy intake (soy foods or soy constituents). **MAIN RESULTS:** Out of 477 articles that met our initial criteria, a total of seven epidemiology studies consisting of five case-control studies and two cohort studies were included in the final analyses. Compared with the lowest soy intake, the OR for the highest soy intake was 0.61 (95% CI, 0.53-0.72) of all endocrine-related cancers among seven studies; 0.70 for endometrial cancer (95% CI, 0.57-0.86) and 0.52 for ovarian cancer (95% CI, 0.42-0.66) in the fixed-effects

meta-analyses. The subgroup analyses by study design showed similar findings among the case-control studies (OR, 0.62; 95% CI, 0.53-0.73) and the cohort studies (OR, 0.57; 95% CI, 0.36-0.90). **AUTHOR'S CONCLUSIONS:** The results of the current study showed protective effects of soy intake on the risk for endocrine-related gynaecological cancers. Additional larger prospective studies are now needed.

Mindfulness-Based Cognitive Therapy

Foley, E, Andrew Baillie, Malcolm Huxter, Melanie Price and Emma Sinclair. **Mindfulness-Based Cognitive Therapy for Individuals Whose Lives have been Affected by Cancer: A Randomized Controlled Trial** *J Consult Clin Psychol*. 2010 02; 781: 72-79.

Objective: This study evaluated the effectiveness of mindfulness-based cognitive therapy (MBCT) for individuals with a diagnosis of cancer. **Method:** Participants (N = 115) diagnosed with cancer, across site and stage, were randomly allocated to either the treatment or the wait-list condition. Treatment was conducted at 1 site, by a single therapist, and involved participation in 8 weekly 2-hr sessions that focused on mindfulness. Participants meditated for up to 1 hr daily and attended an additional full-day session during the course. Participants were assessed before treatment and 10 weeks later; this second assessment occurred immediately after completion of the program for the treatment condition. The treatment condition was also assessed at 3 months postintervention. All postinitial assessments were completed by assessors who were blind to treatment allocation. **Results:** There were large and significant improvements in mindfulness (effect size [ES] = 0.55), depression (ES = 0.83), anxiety (ES = 0.59), and distress (ES = 0.53) as well as a trend for quality of life (ES = 0.30) for MBCT participants compared to those who had not received the training. The wait-list group was assessed before and after receiving the intervention and demonstrated similar change. **Conclusions:** These improvements represent clinically meaningful change and provide evidence for the provision of MBCT within oncology settings.

Prostate Cancer

Hwang, YW, S. Y. Kim, S. H. Jee, Y. N. Kim and C. M. Nam. **Soy Food Consumption and Risk of Prostate Cancer: A Meta-Analysis of Observational Studies.** *Nutrition & Cancer*. 2009 615: 598-606.

Soybean products have been suggested to have a chemo preventive effect against prostate cancer. The aim of this study was to provide a comprehensive meta-analysis on the extent of the possible association between soy-based food consumption and the risk of prostate cancer. Five cohort studies and 8 case-control studies were identified using MEDLINE, EMBASE, CINAHL, Korea Medical Database, KoreaMed, Korean studies Information Service System, Japana Centra Revuo Medicina, China National Knowledge Infrastructure, and a manual search. Summary odds ratios (ORs) comparing high versus low categories of soybean consumptions were calculated on the basis of the random effect model. We analyzed the associations based

on the different types of soybean consumptions. The summary ORs (95% CI) for total soy foods were 0.69 (CI = 0.57-0.84) and 0.75 (CI = 0.62-0.89) for nonfermented soy foods. Among individual soy foods, only tofu yielded a significant value of 0.73 (CI = 0.57-0.92). Consumption of soybean milk, miso, or natto did not significantly reduce the risk of prostate cancer. Genistein and daidzein were associated with a lower risk of prostate cancer. This systematic review suggests that soy food consumption could lower the risk of prostate cancer. This conclusion, however, should be interpreted with caution because various biases can affect the results of a meta-analysis.

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



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Exercise

Galvao, DA, D. R. Taaffe, N. Spry, D. Joseph and R. U. Newton. **Combined Resistance and Aerobic Exercise Program Reverses Muscle Loss in Men Undergoing Androgen Suppression Therapy for Prostate Cancer without Bone Metastases: A Randomized Controlled Trial.** *Journal of Clinical Oncology.* 2010 Jan 10; 282: 340-347.

PURPOSE: Androgen suppression therapy (AST) results in musculoskeletal toxicity that reduces physical function and quality of life. This study examined the impact of a combined resistance and aerobic exercise program as a countermeasure to these AST-related toxicities. **PATIENTS AND METHODS:** Between 2007 and 2008, 57 patients with prostate cancer undergoing AST (commenced > 2 months prior) were randomly assigned to a program of resistance and aerobic exercise (n = 29) or usual care (n = 28) for 12 weeks. Primary end points were whole body and regional lean mass. Secondary end points were muscle strength and function, cardiorespiratory capacity, blood biomarkers, and quality of life. **RESULTS:** Analysis of covariance was used to compare outcomes for groups at 12 weeks adjusted for baseline values and potential confounders. Patients undergoing exercise showed an increase in lean mass compared with usual care (total body, P = .047; upper limb, P < .001; lower limb, P = .019) and similarly better muscle strength (P < .01), 6-meter walk time (P = .024), and 6-meter backward walk time (P = .039). Exercise also improved several aspects of quality of life including general health (P = .022) and reduced fatigue (P = .021) and decreased levels of C-reactive protein (P = .008). There were no adverse events during the testing or exercise intervention program. **CONCLUSION:** A relatively brief exposure to exercise significantly improved muscle mass, strength, physical function, and balance in hypogonadal men compared with normal care. The exercise regimen was well tolerated and could be recommended for patients undergoing AST as an effective countermeasure to these common treatment-related adverse effects.

Study of the Month

Kang, HW, D. Kim, H. J. Kim, et al. **Visceral Obesity and Insulin Resistance as Risk Factors for Colorectal Adenoma: A Cross-Sectional, Case-Control Study.** *Am J Gastroenterol.* 2010 January; 1051: 178-187.

OBJECTIVES: Colorectal adenoma is known to be associated with obesity, but the association between colorectal adenoma and visceral adipose tissue (VAT) area measured by abdominal computed tomography (CT) has not been documented clearly. In addition, the relationship between insulin resistance and colorectal adenomas, which underlies the mechanism that links obesity and colorectal adenoma, has not been studied extensively. The aim of this study was to examine VAT area and insulin resistance as risk factors of colorectal adenoma. **METHODS:** A cross-sectional, case-control study was conducted in Koreans that presented for health check-ups. Subjects underwent various laboratory tests, abdominal CT, and colonoscopy. VAT, subcutaneous adipose tissue (SAT), and homeostatic metabolic assessment (HOMA) index were evaluated as potential risk factors of colorectal adenoma in 2,244 age- and sex-matched subjects. **RESULTS:** According to univariate analysis, the prevalences of smoking, hypertension, metabolic syndrome, and family history of colorectal cancer were higher in the adenoma group than in the normal control group. In addition, body mass index, waist circumference, triglyceride, high-density lipoprotein cholesterol, and VAT and SAT areas were significantly different in the two groups. According to the multivariate analysis adjusted for multiple confounders, VAT area was independently associated with the risk of colorectal adenoma (odds ratio (OR) 3.09, 95% confidence interval (CI): 2.19-4.36, highest quintile vs. lowest quintile). Mean HOMA index was higher in the adenoma group than in the control group (OR 1.99, 95% CI: 1.35-2.92, highest vs. lowest quintile). **CONCLUSIONS:** Visceral obesity was found to be an independent risk factor of colorectal adenoma, and insulin resistance was associated with the presence of colorectal adenoma.

InspireHealth provides an integrated whole person approach to health for individuals living with cancer. Our medical doctors guide patients to explore and learn about a variety of wellness approaches to health and healing in addition to conventional cancer treatment. This integrated medical model, which engages people in their own care, improves quality of life and reduces the likelihood of cancer recurrence. The editorial board includes: Dr. Hal Gunn, CEO and Co-founder, Dr. Janice Wright, Dr. Teresa Clarke, Dr. Ron Puhky, Dr. Walter Lemmo, ND, and Julius Halaschek-Wiener, PhD.

Jan Rennie and Dr. Julius Halaschek-Wiener, PhD compile InspireHealth's Research Updates with guidance from the editorial board.

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