



# REsearch UPDATES

FOR THE LATEST IN WORLDWIDE INTEGRATIVE CANCER CARE

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**IN THIS ISSUE:** There were a number of studies about psychosocial aspects of cancer – Yu and Bernstein found that patients with brain tumors prefer to have all of the information that they can when it comes to treatment-related decision making (even if they ultimately let their doctor decide); Xu et al. found that when men with prostate cancer weighed the pros and cons of any particular treatment, they ultimately made the best decision that they could based on the information given to them; and Schmid-Buchi and colleagues found that cancer patients and their relatives needed additional psychological support after patients had finished their treatment. In other studies, Truong and associates reported that moderate-intensity walking was safe and beneficial for patients with prostate cancer undergoing radical external beam radiotherapy. Parry and associates reported that reducing one's fat intake may prevent breast cancer. Stevens et al. found that intake of high levels of folate reduced the risk of colorectal cancer, and could not find evidence to indicate that supplementation or fortification increased the risk. Jang and colleagues reported that women who smoked and had cancer had a worse quality of life than those who had cancer but had either never smoked, or had quit smoking. Jane and associates found that massage therapy was useful for cancer patients with metastatic bone pain. In our study of the month, Vrieling et al. found that a lower level of vitamin D is associated with poorer overall survival and disease-free survival in postmenopausal breast cancer patients.

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## PROSTATE CANCER



Truong, P.T., Gaul, C.A., McDonald, R.E. et al.

### Prospective evaluation of a 12-week walking exercise program and its effect on fatigue in prostate cancer patients undergoing radical external beam radiotherapy.

*American Journal of Clinical Oncology*. 2011 Aug; 34(4): 350-355.

**OBJECTIVE:** To evaluate tolerability and compliance to a walking exercise program and its effect on fatigue during and after radical external beam radiation therapy (EBRT) for prostate cancer. **METHODS:** A total of 50 subjects with prostate cancer undergoing EBRT over 6 to 8 weeks were prospectively accrued to an exercise intervention group, matched for age and clinical characteristics to 30 subjects in a historical control group who underwent EBRT with no specific exercise intervention. Starting 1 week before EBRT, exercise participants performed moderate-intensity walking targeting 60% to 70% age-predicted maximum heart rate, at least 20 min/d, 3 d/wk over 12 weeks. The Brief Fatigue Inventory was administered at baseline, mid-EBRT (week 3-4), end-EBRT (week 6-8), and 6 months post-EBRT.

**RESULTS:** Of 50, 42 (84%) of exercise participants completed the walking program. There were no cardiovascular complications, musculoskeletal injuries, or other adverse events. A total of 89% subjects reported "Good-Excellent" satisfaction during and up to 6 months post-EBRT. Fatigue in control subjects escalated from baseline to end-EBRT, remaining high at 6 months post-EBRT ( $P[r] = 0.03$ ). In contrast, mean total fatigue scores in exercise subjects were stable from baseline up to 6 months post-EBRT ( $P = 0.52$ ). Trends for higher fatigue interference with quality of life were observed in the control group as compared with the exercise group.



**CONCLUSIONS:** Moderate-intensity walking exercise during radical EBRT is safe and feasible. The high convenience and satisfaction ratings, in conjunction with the observed fatigue trends, indicate that this activity has the potential to attenuate fatigue and improve quality of life for patients with localized prostate cancer undergoing curative therapy.

## BREAST CANCER

Parry, B.M., Milne, J.M., Yadegarfar, G. et al.

### **Dramatic dietary fat reduction is feasible for breast cancer patients: Results of the randomised study, WINS (UK) – Stage 1.**

*European Journal of Surgical Oncology.* 2011 Oct; 37(10): 848-855.

**INTRODUCTION:** The influence of dietary fat on breast tumour growth<sup>1</sup> and, more recently, on treatment outcomes,<sup>2,3</sup> suggests an important role for dietary advice in the future health of breast cancer patients. The Women's Intervention Nutrition Study (UK) - Stage 1 assessed the feasibility of achieving and maintaining a  $\geq 50\%$  reduction in reported fat intake in postmenopausal, early stage breast cancer patients in the UK. **METHOD:** This study recruited patients in South-east England between 2000 and 2005. They were randomly allocated into two groups. Group 1 (n = 54), received specific dietary counselling to halve their reported fat intake and maintain this low fat intake. Group 2 (n = 53) received healthy eating advice only. Dietitian-led group sessions provided support for women in both groups over 2 years. 4 Validated four-day diaries were used to measure intake. Data analysis used Generalised Linear Model (GLM) for repeated measures and logistic regression.

**RESULTS:** A significantly greater proportion of women in Group 1 reported a fat intake reduction of  $\geq 50\%$  at 3 months (p < .001) and 24 months (p < .001) than in Group 2. The size of the effect of active dietary counselling was 37% at 3 months (95%CI: 21-54%) and 35% at 24 months (95%CI: 17-53%). Mean fat intake was halved at 3 months and 24 months in Group 1 only.

**CONCLUSION:** Demonstrating such feasibility is a key step towards defining diet's role in the secondary prevention of breast cancer.

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Larsen, S.B., Olsen, A., Lynch, J. et al.

### **Socioeconomic position and lifestyle in relation to breast cancer incidence among postmenopausal women: a prospective cohort study, Denmark, 1993-2006.**

*Cancer Epidemiology.* 2011 Oct; 35(5): 438-441.

**BACKGROUND:** In Denmark, the incidence of breast cancer is higher among women with higher socioeconomic position. We investigated whether differences in exposure to certain risk factors contribute to this gradient, as measured from education, income and occupation. **METHODS:** We conducted a cohort study of 23,111 postmenopausal women aged 50-65 years who were enrolled in the prospective Danish 'Diet, Cancer and Health' study between 1993 and 1995. At baseline, all women filled in a questionnaire on lifestyle and food frequency. The results were analysed in Cox proportional hazard models.

**RESULTS:** Part of the association with socioeconomic position is due to the potential mediators reproductive pattern, use of hormone replacement therapy and alcohol consumption. After simultaneous adjustment for these factors, the hazard ratios were 1.06 (95% confidence interval [CI], 0.88-1.27) for women with higher education and 1.07 (95% CI, 0.85-1.34) for women with higher income. The HR ratio for women working as higher officials when compared with unskilled workers was 1.23 (0.96-1.59).

**CONCLUSION:** The results support the hypothesis that the higher incidence of breast cancer among socially advantaged women is mediated partly by differences in exposure to reproductive factors, hormone replacement therapy and alcohol.



## COLORECTAL CANCER

Hu, Y., McIntosh, G.H., Le Leu, R.K. et al.

### The influence of selenium-enriched milk proteins and selenium yeast on plasma selenium levels and rectal selenoprotein gene expression in human subjects.

*British Journal of Nutrition.* 2011 Aug; 106(4): 572-582.

**BACKGROUND:** Certain forms of dietary Se may have advantages for improving human Se status and regulating the risk for disease, such as cancers, including colorectal cancer (CRC). The present study compared the effects of a Se-enriched milk protein (dairy-Se) with a Se-rich yeast (yeast-Se) on plasma Se levels and rectal selenoprotein gene expression since we reasoned that if these genes were not regulated, there was little potential for regulating the risk for CRC in this organ.

**METHODS:** A total of twenty-three healthy volunteers with plasma Se in the lower half of the population range were supplemented with dairy-Se (150 mug/d) or yeast-Se (150 mug/d) for 6 weeks, followed by 6 weeks of washout period. Blood was sampled every 2 weeks, and rectal biopsies were obtained before and after Se supplementation and after the washout period. Plasma Se levels and glutathione peroxidase (GPx) activity, and rectal mRNA of selenoprotein P (SeP), cytosolic GPx-1 (GPx-1), gastrointestinal GPx-2 (GPx-2) and thioredoxin reductase-1 (TrxR-1) were measured.

**RESULTS:** Plasma Se levels increased rapidly in both Se groups ( $P < 0.001$ ); plasma GPx activity was not significantly changed. Rectal SeP mRNA increased at 6 weeks compared with baseline in both Se groups ( $P < 0.05$ ); only dairy-Se resulted in a sustained elevation of SeP after the washout period ( $P < 0.05$ ). Rectal GPx-1 and GPx-2 mRNA were higher with dairy-Se ( $P < 0.05$ ) than with yeast-Se at 6 weeks.

**CONCLUSION:** In conclusion, three rectal selenoprotein mRNA were differentially regulated by dairy-Se and yeast-Se. Changes in rectal selenoproteins are not predicted by changes in plasma Se; dairy-Se effectively regulates the expression of several rectal selenoproteins of relevance to the risk for CRC.

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Stevens, V.L., McCullough, M.L., Sun, J. et al.

### High levels of folate from supplements and fortification are not associated with increased risk of colorectal cancer.

*Gastroenterology.* 2011; 141(10):98-105.

**BACKGROUND & AIMS:** Folate intake has been inversely associated with colorectal cancer risk in several prospective epidemiologic studies. However, no study fully assessed the influence of the high levels of folate that are frequently consumed in the United States as a result of mandatory folate fortification, which was fully implemented in 1998, and the recent increase in use of folate-containing supplements. There is evidence that consumption of high levels of folic acid, the form of folate used for fortification and in supplements, has different effects on biochemical pathways than natural folates and might promote carcinogenesis. **METHODS:** We investigated the association between folate intake and colorectal cancer among 43,512 men and 56,011 women in the Cancer Prevention Study II (CPS-II) Nutrition Cohort; 1023 were diagnosed with colorectal cancer between 1999 and 2007, a period entirely after folate fortification began. Cox proportional hazards regression was used to calculate multivariate hazards ratios (RR) and 95% confidence interval (CI).

**RESULTS:** Intake of high levels of natural folate (RRQ5vsQ1=0.86; 95% CI: 0.70-1.06;  $P$  trend=.12) or folic acid (RRQ5vsQ1=0.84; 95% CI: 0.68-1.03;  $P$  trend=.06) were not significantly associated with risk of colorectal cancer. Total folate intake was significantly associated with lower risk (RRQ5vsQ1=0.81; 95% CI: 0.66-0.99;  $P$  trend=.047).

**CONCLUSIONS:** Intake of high levels of total folate reduces risk of colorectal cancer; there is no evidence that dietary fortification or supplementation with this vitamin increases colorectal cancer risk.



## SMOKING

Jang, S., Prizment, A., Haddad, T. et al.

### Smoking and quality of life among female survivors of breast, colorectal and endometrial cancers in a prospective cohort study.

*Journal of Cancer Survivorship.* 2011 Jun; 5(2): 115-122.

**PURPOSE:** To examine the association of smoking and quality of life (QOL) among survivors of breast, colorectal, or endometrial cancers. **METHODS:** The study included women who joined the Iowa Women's Health Study in 1986 and were subsequently diagnosed with breast, colorectal, or endometrial cancer through 2004 (n = 1920). Smoking status was reported at baseline and in 2004; QOL was assessed in 2004 using the Medical Outcomes Study Short Form-36. Multivariate-adjusted odds ratios were calculated to examine the associations of smoking status and poor QOL (score lower than one-half a standard deviation below the mean of the non-smokers).

**RESULTS:** Compared with non-smokers, persistent smokers had higher likelihood of reporting poor Physical Functioning (odds ratio [OR] = 2.40, 95% confidence interval [CI] = 1.32-4.37), Mental Health (OR = 1.92, CI = 1.09-3.40), and Role Emotional (OR = 2.01, CI = 1.10-3.66), whereas former smokers had higher likelihood of reporting poor Physical Functioning (OR = 1.65, CI = 1.10-2.45), Mental Health (OR = 1.62, CI = 1.11-2.37), and General Health (OR = 1.51, CI = 1.03-2.21). A statistically significant trend toward higher likelihood of poor QOL was observed across smoking groups in Vitality, Physical Functioning, Mental Health, and Role Emotional. Further adjustment for physical activity resulted in attenuation of the odds ratios and p-values for trend.

**CONCLUSION:** Among women with breast, colorectal, or endometrial cancers, smokers were more likely than former or non-smokers to have poor QOL. Physical activity explained, in part, the association between smoking status and QOL in our study.

## MASSAGE

Jane, S.-W., Chen, S.-L., Wilkie, D.J. et al.

### Effects of massage on pain, mood status, relaxation, and sleep in Taiwanese patients with metastatic bone pain: A randomized clinical trial.

*Pain.* 2011 Oct; 152(10): 2432-2442.

**BACKGROUND:** To date, patients with bony metastases were only a small fraction of the samples studied, or they were entirely excluded. Patients with metastatic cancers, such as bone metastases, are more likely to report pain, compared to patients without metastatic cancer (50-74% and 15%, respectively). Their cancer pain results in substantial morbidity and disrupted quality of life in 34-45% of cancer patients. Massage therapy (MT) appears to have positive effects in patients with cancer; however, the benefits of MT, specifically in patients with metastatic bone pain, remains unknown. **METHODS:** The purpose of this randomized clinical trial was to compare the efficacy of MT to a social attention control condition on pain intensity, mood status, muscle relaxation, and sleep quality in a sample (n = 72) of Taiwanese cancer patients with bone metastases.

**RESULTS:** In this investigation, MT was shown to have beneficial within- or between-subjects effects on pain, mood, muscle relaxation, and sleep quality. Results from repeated-measures analysis of covariance demonstrated that massage resulted in a linear trend of improvements in mood and relaxation over time. More importantly, the reduction in pain with massage was both statistically and clinically significant, and the massage-related effects on relaxation were sustained for at least 16-18 hours postintervention. Furthermore, massage-related effects on sleep were associated with within-subjects effects. Future studies are suggested with increased sample sizes, a longer interventional period duration, and an objective and sensitive measure of sleep.

**CONCLUSION:** Overall, results from this study support employing MT as an adjuvant to other therapies in improving bone pain management.



## PSYCHOSOCIAL

Yu, J.J., Bernstein, M.

### Brain tumor patients' views on deception: A qualitative study.

*J. Neurooncol.* 2011 Aug; 104(1): 331-337.

**BACKGROUND:** Given the trust the public places in the medical profession, the question of when it might be acceptable to minimally deceive patients, in their best interests, is a challenging one to answer.

**METHODS:** In this study, we explore neuro-oncology patients' attitudes towards dilemmas in which they may feel deceived, and with that information make recommendations on what steps physicians can take to avoid breaking that trust. Qualitative case study methodology was used. Thirty-two face-to-face interviews with post-operative brain tumor patients were conducted and recorded. Interviews were transcribed and subjected to modified thematic analysis. The majority of patients had a postsecondary education, and there was substantial religious and ethnic diversity among them.

**RESULTS:** Five prominent themes arose from the analysis: (1) patients are hesitant about trainees working on their case, but they are more open to it if they expect the occurrence ahead of time; (2) patients wish to know the exact details when an error has occurred, even if it is of inconsequential effect for them; (3) patients generally prefer to know exactly what the doctor knows, even if nothing can be changed; (4) patients expect physicians to provide them with all the options and resources available; and (5) there are special cases in which patients accept a delay in knowing. Most neuro-oncology patients trust their physicians to make the best decisions for them, but that does not mean they would accept subtle forms of deception.

**CONCLUSION:** Patients prefer to have all the information necessary in order to make their own decision.



Xu, J., Dailey, R.K., Egely, S. et al.

### Men's perspectives on selecting their prostate cancer treatment.

*J. Natl. Med. Assoc.* 2011 Jun; 103(6): 468-478.

**OBJECTIVE:** In the context of scientific uncertainty, treatment choices for localized prostate cancer vary, but reasons for this variation are unclear. We explored how black and white American men made their treatment decision. **METHODS:** Guided by conceptual model, we conducted semistructured interviews of 21 American (14 black and 7 white) men with recently diagnosed localized prostate cancer.

**RESULTS:** Physician recommendation was very important in the treatment decision, but patient self-perception/values and attitudes/beliefs about prostate cancer were also influential. Patients who chose surgery believed it offered the best chance of cure and were more concerned that the cancer might spread if not surgically removed. Patients who chose radiation therapy believed it offered equal efficacy of cure but fewer side effects than surgery. Fear of future consequences was the most common reason to reject watchful waiting. Anecdotal experiences of family and friends were also important, especially in deciding "what not to do." The new technology of robotic-assisted prostatectomy provided optimism for men who wanted surgery but feared morbidity associated with traditional open surgery. Few men seemed aware that treatment did not guarantee improved survival.

**CONCLUSION:** Most men reported making "the best choice for me" by taking into account medical information and personal factors. Perceptions of treatment efficacy and side effects, which derived mainly from physicians' descriptions and/or anecdotal experiences of family and friends, were the most influential factors in men's treatment decision. By understanding factors that influence patients' treatment decisions, clinicians may be more sensitive to individual patients' preferences/concerns and provide more patient-centered care.





Schmid-Buchi, S., Halfens, R.J., Dassen, T. et al.

### Psychosocial problems and needs of posttreatment patients with breast cancer and their relatives.

*European Journal of Oncology Nursing*. 2011 Jul; 15(3): 260-266.

**PURPOSE:** The study assessed and compared the psychosocial needs of patients with breast cancer and of their relatives, the patients' and relatives' burden of illness, anxiety, depression and distress and assessed the patients' cancer treatment-related symptoms and identified relevant factors influencing patients' and relatives' needs. **METHOD:** Seventy-two patients (n=72) participated with a relative in a cross-sectional mail-survey, 1-22 months after cancer treatment.

**RESULTS:** The patients reported needing help with psychological and sexual issues. They suffered from treatment-related symptoms. More treatment-related symptoms and depression were related to the patients' needs for supportive care. Their relatives' needs primarily concerned access to information and communication with health care professionals. Relatives had higher levels of anxiety (25.0% vs. 22.2%), depression (12.5% vs. 8.3%) and distress (40% vs. 34%) than patients. Higher levels of depression, younger age and having a disease themselves were associated with relatives' need for help.

**CONCLUSION:** Patients' and relatives' substantial needs and psychological problems require professional support even after completion of the patients' treatment. Continued assessment of the patients' and their relatives' needs and of the patients' symptoms provide the basis for purposeful counselling and education. Rehabilitation programs for patients and their relatives should be developed and implemented in clinical practice.

## STUDY OF THE MONTH

Vrieling, A., Hein, R., Abbas, S. et al.

### Serum 25-hydroxyvitamin D and postmenopausal breast cancer survival: a prospective patient cohort study.

*Breast Cancer Res*. 2011 Jul 26; 31(4): R74.

**INTRODUCTION:** Vitamin D has been postulated to be involved in cancer prognosis. Thus far, only two studies reported on its association with recurrence and survival after breast cancer diagnosis yielding inconsistent results. Therefore, the aim of our study was to assess the effect of post-diagnostic serum 25-hydroxyvitamin D [25(OH)D] concentrations on overall survival and distant disease-free survival.

**METHODS:** We conducted a prospective cohort study in Germany including 1,295 incident postmenopausal breast cancer patients aged 50-74 years. Patients were diagnosed between 2002 and 2005 and median follow-up was 5.8 years. Cox proportional hazards models were stratified by age at diagnosis and season of blood collection and adjusted for other prognostic factors. Fractional polynomials were used to assess the true dose-response relation for 25(OH)D.

**RESULTS:** Lower concentrations of 25(OH)D were linearly associated with higher risk of death (hazard ratio (HR) = 1.08 per 10 nmol/L decrement; 95% confidence interval (CI), 1.00 to 1.17) and significantly higher risk of distant recurrence (HR = 1.14 per 10 nmol/L decrement; 95%CI, 1.05 to 1.24). Compared with the highest tertile ( $\geq 55$  nmol/L), patients within the lowest tertile ( $< 35$  nmol/L) of 25(OH)D had a HR for overall survival of 1.55 (95%CI, 1.00 to 2.39) and a HR for distant disease-free survival of 2.09 (95%CI, 1.29 to 3.41). In addition, the association with overall survival was found to be statistically significant only for 25(OH)D levels of blood samples collected before start of chemotherapy but not for those of samples taken after start of chemotherapy (P for interaction = 0.06).

**CONCLUSIONS:** In conclusion, lower serum 25(OH)D concentrations may be associated with poorer overall survival and distant disease-free survival in postmenopausal breast cancer patients.

## FOR FURTHER READING ON THE WEB:

## PROSTATE CANCER



Shahar, S., Shafurah, S., Shaari, N.S.A.H. et al.

### Roles of diet, lifetime physical activity and oxidative DNA damage in the occurrence of prostate cancer among men in Klang Valley, Malaysia.

*Asian Pacific Journal of Cancer Prevention.* 2011; 12(3): 605-611.

**BACKGROUND:** There is a paucity of information on risk factors of prostate cancer, especially those related to dietary and lifestyle among Asian populations. **OBJECTIVE:** This study aimed to determine the relationship between dietary intake (macronutrients, fruits, vegetables and lycopene), lifetime physical activity and oxidative DNA damage with prostate cancer. **DESIGN:** A case control study was carried out among 105 subjects (case n=35, control n=70), matched for age and ethnicity. Data on sociodemographic, medical, dietary intake, consumption of lycopene rich food and lifetime physical activity were obtained through an interview based questionnaire. Anthropometric measurements including weight, height and waist hip circumferences were also carried out on subjects. A total of 3 mL fasting venous blood was drawn to assess lymphocyteoxidative DNA damage using the alkaline comet assay.

**RESULTS:** Cases had a significantly higher intake of fat ( $27.7 \pm 5.5\%$ ) as compared to controls ( $25.1 \pm 5.9\%$ ) ( $p < 0.05$ ). Mean intakes of fruits and vegetables ( $3.11 \pm 1.01$  servings/d) ( $p < 0.05$ ), fruits ( $1.23 \pm 0.59$  servings/d) ( $p < 0.05$ ) and vegetables ( $1.97 \pm 0.94$  servings/d) were higher in controls than cases ( $2.53 \pm 1.01$ ,  $0.91 \pm 0.69$ ,  $1.62 \pm 0.82$  servings/d). A total of 71% of cases did not meet the recommendation of a minimum of three servings of fruits and vegetables daily, as compared to 34% of controls ( $p < 0.05$ ) (adjusted OR 6.52 (95% CI 2.3-17.8)) ( $p < 0.05$ ). Estimated lycopene intake among cases ( $2,339 \pm 1,312$  mcg/d) were lower than controls ( $3881 \pm 3120$  mcg/d) ( $p < 0.01$ ). Estimated lycopene intake of less than 2,498 mcg/day (50th percentile) increased risk of prostate cancer by double [Adjusted OR 2.5 (95%CI 0.99-6.31)]. Intake of tomatoes, watermelon, guava, pomelo, papaya, mango, oranges, dragon fruit, carrot, tomato sauce and barbeque sauce were higher in controls compared to cases. Intake of tomato sauce of more than 2.24 g/d (25th percentile), papaya more than 22.7 g/d (50th percentile) and oranges more than 19.1g/h (50th percentile) reduced prostate cancer risk by 7.4 (Adjusted OR 7.4 (95% CI 1.17-46.8)), 2.7 (adjusted OR 2.75 (95% CI 1.03-7.39)) and 2.6 times (adjusted OR = 2.6 (95% CI=1.01-6.67)), respectively ( $p < 0.05$  for all parameters). No oxidative damage was observed among subjects. Past history of not engaging with any physical activities at the age of 45 to 54 years old increased risk of prostate cancer by approximately three folds (Adjusted OR 2.9(95% CI = 0.8-10.8)) ( $p < 0.05$ ).

**CONCLUSION:** In conclusion, low fat diet, high intake of fruits, vegetables and lycopene rich foods and being physically active at middle age were found to be protective. Thus, it is essential for Malaysian men to consume adequate fruits and vegetables, reduce fat intake and engage in physical activity in order to reduce prostate cancer risk.

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



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