

# REsearch UPDATES

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**IN THIS ISSUE:** Landberg et al. found that whole grain and bran from rye reduced plasma PSA levels. Houston and associates found that narrative storytelling had a favourable effect on blood pressure, and it may have a favourable impact on cancer outcomes. Jeong et al. found that combining an Oriental herbal formula with conventional therapy could prolong the lives of lung cancer patients. Lee found that an herbal remedy improved appetite and body weight in anorexic cancer patients. In our study of the month, Engel et al. found that there is a threshold of vitamin D from sunlight and supplementation that is required to prevent breast cancer, and that this threshold might be difficult to reach in Northern latitudes where the quality of sunlight is too poor for adequate vitamin D production.

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## PROSTATE CANCER

Landberg, R, S. O. Andersson, J. X. Zhang, et al.

### Rye Whole Grain and Bran Intake Compared with Refined Wheat Decreases Urinary C-Peptide, Plasma Insulin, and Prostate Specific Antigen in Men with Prostate Cancer.

*J Nutr.* 2010 Dec; 14012: 2180-2186.

**BACKGROUND:** Rye whole grain and bran intake has shown beneficial effects on prostate cancer progression in animal models, including lower tumor take rates, smaller tumor volumes, and reduced prostate specific antigen (PSA) concentrations. A human pilot study showed increased apoptosis after consumption of rye bran bread. **METHODS:** In this study, we investigated the effect of high intake of rye whole grain and bran on prostate cancer progression as assessed by PSA concentration in men diagnosed with prostate cancer. Seventeen participants were provided with 485g rye whole grain and bran products (RP) or refined wheat products with added cellulose (WP), corresponding to ~50% of daily energy intake, in a randomized controlled, crossover design. Blood samples were taken from fasting men before and after 2, 4, and 6 wk of treatment and 24-h urine samples were collected before the first intervention period and after treatment.

**RESULTS:** Plasma total PSA concentrations were lower after treatment with RP compared with WP, with a mean treatment effect of -14% (P = 0.04). Additionally, fasting plasma insulin and 24-h urinary C-peptide excretion were lower after treatment with RP compared with WP (P < 0.01 and P = 0.01, respectively). Daily excretion of 5 lignans was higher after the RP treatment than after the WP treatment (P < 0.001).

**CONCLUSION:** We conclude that whole grain and bran from rye resulted in significantly lower plasma PSA compared with a cellulose-supplemented refined wheat diet in patients with prostate cancer. The effect may be related to inhibition of prostate cancer progression caused by decreased exposure to insulin, as indicated by plasma insulin and urinary C-peptide excretion.



Dunn, BK, E. S. Richmond, L. M. Minasian, et al.

### A Nutrient Approach to Prostate Cancer Prevention: The Selenium and Vitamin E Cancer Prevention Trial (SELECT)

*Nutrition & Cancer.* 2010 Oct; 627: 896-918.

**BACKGROUND:** The Selenium and Vitamin E Cancer Prevention Trial (SELECT) randomized 35,533 healthy men, >55 yr old (>50 yr if African American), with normal digital rectal exams and prostate specific antigens <4 ng/ml to 1) 200 g/day l-selenomethionine, 2) 400 IU/day all-rac-alpha-tocopheryl acetate (vitamin E), 3) both supplements, or 4) placebo for 7 to 12 yr. **METHODS:** The hypotheses underlying SELECT, that selenium and vitamin E individually and together decrease prostate cancer incidence, derived from epidemiologic and laboratory evidence and significant secondary endpoints in the Nutritional Prevention of Cancer (selenium) and Alpha-Tocopherol Beta-Carotene (vitamin E) trials.

**RESULTS:** In SELECT, prostate cancer incidence did not differ among the 4 arms: hazard ratios [99% confidence intervals (CIs)] for prostate cancer were 1.13 (99% CI = 0.95-1.35, P = 0.06; n = 473) for vitamin E, 1.04 (99% CI = 0.87-1.24, P = 0.62; n = 432) for selenium, and 1.05 (99% CI = 0.88-1.25, P = 0.52; n = 437) for selenium + vitamin E vs. 1.00 (n = 416) for placebo. Statistically nonsignificant increased risks of prostate cancer with vitamin E alone [relative risk (RR) = 1.13, P = 0.06] and newly diagnosed Type 2 diabetes mellitus with selenium alone (RR = 1.07, P = 0.16) were observed.

**CONCLUSION:** SELECT data show that neither selenium nor vitamin E, alone or together, in the doses and formulations used, prevented prostate cancer in this heterogeneous population of healthy men.

## BREAST CANCER

Meulepas, JM, P. A. Newcomb, A. N. Burnett-Hartman, et al.

### Multivitamin Supplement use and Risk of Invasive Breast Cancer.

*Public Health Nutr.* 2010 Oct; 1310: 1540-1545.

**OBJECTIVE:** Multivitamin supplements are used by nearly half of middle-aged women in the USA. Despite this high prevalence of multivitamin use, little is known about the effects of multivitamins on health outcomes, including cancer risk. Our main objective was to determine the association between multivitamin use and the risk of breast cancer in women. **DESIGN:** We conducted a population-based case-control study among 2968 incident breast cancer cases (aged 20-69 years), diagnosed between 2004 and 2007, and 2982 control women from Wisconsin, USA. All participants completed a structured telephone interview which ascertained supplement use prior to diagnosis, demographics and risk factor information. Odds ratios and 95 % confidence intervals were calculated using multivariable logistic regression.

**RESULTS:** Compared with never users of multivitamins, the OR for breast cancer was 1.02 (95 % CI 0.87, 1.19) for current users and 0.99 (95 % CI 0.74, 1.33) for former users. Further, neither duration of use (for > or =10 years: OR = 1.13, 95 % CI 0.93, 1.38, P for trend = 0.25) nor frequency (>7 times/week: OR = 1.00, 95 % CI 0.77, 1.28, P for trend = 0.97) was related to risk in current users. Stratification by menopausal status, family history of breast cancer, age, alcohol, tumour staging and postmenopausal hormone use did not significantly modify the association between multivitamin use and breast cancer.

**CONCLUSIONS:** The current study found no association between multivitamin supplement use and breast cancer risk in women.

Thomson, CA, C. L. Rock, P. A. Thompson, et al.

### Vegetable Intake is Associated with Reduced Breast Cancer Recurrence in Tamoxifen Users: A Secondary Analysis from the Women's Healthy Eating and Living Study.

*Breast Cancer Res Treat.* 2011 January; 1252: 519-527.

**BACKGROUND:** The protective effect of vegetables on the risk of breast cancer recurrence is uncertain. **METHODS:** We sought to evaluate the association between breast cancer recurrence and vegetable intake including analyses stratified on tamoxifen use. Experimental evidence of anti-carcinogenic activity of phytochemicals in cruciferous vegetables in combination with tamoxifen led to specific evaluation of this



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class of vegetables as well. To assess the association between vegetable intake and breast cancer recurrence, vegetable intake from repeat 24-h dietary recalls were examined as a secondary analysis of 3,080 breast cancer survivors enrolled in the Women's Healthy Eating and Living (WHEL) Study. At the time of enrollment women were, on average, 23.5 months post-diagnosis. The hazard of recurrence, controlling for relevant and significant clinical and demographic variables, with vegetable intake was assessed overall and separately for women taking tamoxifen.

**RESULTS:** WHEL participants reported mean baseline intakes ( $\bar{x}$ , SE) of 3.1 +/- 0.05 and 0.5 +/- 0.02 servings/day of total and cruciferous vegetables, respectively. Baseline vegetable intake in the highest as compared to lowest tertiles was associated with an overall lower adjusted hazard ratios (HR) for recurrence of 0.69, 95% CI 0.55-0.87. Among women taking tamoxifen, the HRs were 0.56, 95% CI 0.41-0.77 for total vegetables and 0.65, 95% CI 0.47-0.89 for cruciferous vegetable intake. The hazard in women using tamoxifen who reported cruciferous vegetable intake above the median and who were within the highest tertile of total vegetable intake was HR 0.48; 95% CI 0.32-0.70.

**CONCLUSION:** This secondary analysis in over 3,000 breast cancer survivors suggests that baseline vegetable intake may be associated with a reduction in the risk of breast cancer recurrent or new events particularly for those using tamoxifen. Such associations should be explored further as the possibility that vegetable intake is simply a surrogate for other health-promoting behaviors cannot be ruled out.

## COLORECTAL CANCER

Bao, Y, K. Nimptsch, J. A. Meyerhardt, et al.

### Dietary Insulin Load, Dietary Insulin Index, and Colorectal Cancer.

*Cancer Epidemiology Biomarkers and Prevention.* 2010 December; 1912: 3020-3026.

**BACKGROUND:** Circulating insulin levels have been positively associated with risk of colorectal cancer; however, it remains unclear whether a diet inducing an elevated insulin response influences colorectal cancer risk. On the basis of a novel insulin index for individual foods, we estimated insulin demand for overall diets and assessed its association with colorectal cancer in the Nurses' Health Study and Health Professionals Follow-up Study. **METHODS:** We followed 86,740 women and 46,146 men who were free of cancer and diabetes at baseline and identified a total of 2,481 colorectal cancer cases during up to 26 years of follow-up. Dietary insulin load was calculated as a function of food insulin index and the energy content of individual foods was reported on food frequency questionnaires. Average dietary insulin index was calculated by dividing the dietary insulin load by the total energy intake.

**RESULTS:** Dietary insulin load and dietary insulin index were not associated with risk of colorectal cancer. Comparing the highest with the lowest quintiles, the pooled multivariate relative risks of colorectal cancer were 0.91 (95% CI = 0.79-1.05) for dietary insulin load and 0.93 (95% CI = 0.81-1.08) for dietary insulin index. Body mass index and physical activity did not modify the association of dietary insulin load or index with colorectal cancer.

**CONCLUSION:** A diet high in foods that increase postprandial insulin levels did not increase the risk of colorectal cancer in this large prospective study.

**IMPACT:** This study is the first to investigate insulin index and load in relation to colorectal cancer.

## PANCREATIC CANCER

Bravi, F, J. Polesel, C. Bosetti, et al.

### Dietary Intake of Selected Micronutrients and the Risk of Pancreatic Cancer: An Italian Case-Control Study.

*Annals of Oncology.* 2011; 221: 202-206.

**OBJECTIVE:** Several studies have shown an inverse relation between vegetable and fruit intake and pancreatic cancer, but no specific beneficial component of such foods has been consistently identified. We considered the role of 15 selected vitamins and carotenoids and 6 minerals on pancreatic cancer risk in an Italian case-control study. **METHODS:** Subjects were 326 patients with incident pancreatic cancer and 652



controls, admitted to the same hospitals as cases for acute conditions. Micronutrient computation was based on a validated and reproducible food-frequency questionnaire. We estimated the odds ratios (OR) and confidence intervals (CI) using conditional logistic regression models, adjusted for various confounding factors and for energy intake, according to the residual model.

**RESULTS:** Comparing the highest to the lowest quintile of intake, the OR were 0.60 (95% CI 0.36-0.98) for vitamin E, 0.44 (95% CI 0.27-0.73) for vitamin C, 0.56 (95% CI 0.34-0.93) for folate, and 0.57 (95% CI 0.35-0.92) for potassium. No significant inverse associations were observed for alpha-carotene (OR = 0.69, 95% CI 0.43-1.12), beta-carotene (OR = 0.64, 95% CI 0.39-1.06), and beta-cryptoxanthin (OR = 0.66, 95% CI 0.39-1.09). No relation was found for other micronutrients considered.

**CONCLUSION:** Our findings support a favorable role of vitamins E and C, selected carotenoids, and folate on pancreatic carcinogenesis.

## ENDOMETRIAL CANCER

Cui, X, B. Rosner, W. C. Willett et al.

### Antioxidant Intake and Risk of Endometrial Cancer: Results from the Nurses' Health Study.

*International Journal of Cancer.* 2011 01 Mar 2011; 1285: 1169-1178.

**BACKGROUND:** To investigate the associations between antioxidant intake and risk of endometrial cancer, the authors analyzed data from the prospective Nurses' Health Study. From 1980 to 2006, 669 invasive adenocarcinoma cases were identified over 1.3 million person-years of follow-up. **METHODS:** Information on dietary intake was collected in 1980 and updated every 2-4 years. Cox proportional hazard models were used to calculate the multivariate relative risks (RR), controlling for total energy and potential risk factors for endometrial cancer.

**RESULTS:** Overall, the authors found no association between intakes of vitamins A, C, E or carotenoids from foods or supplements and cancer risk. The RR and 95% confidence intervals (CI) for the highest vs. lowest quintiles of vitamins A, C, E and total carotenoids were 1.09 (95% CI: 0.85-1.39), 0.98 (95% CI: 0.76-1.25), 1.07 (95% CI: 0.83-1.38) and 1.12 (95% CI: 0.86-1.45), respectively. Similarly, the use of multivitamins or specific vitamins A, C or E supplements was unassociated with risk. In subgroup analyses, several associations seemed to vary by postmenopausal hormone use.

**CONCLUSION:** Our results suggest that there is no overall association between dietary antioxidant intake or use of antioxidant supplements with risk of endometrial cancer.

## STORYTELLING

Houston, TK, J. J. Allison, M. Sussman, et al.

### Culturally Appropriate Storytelling to Improve Blood Pressure: A Randomized Trial.

*Ann Intern Med.* 2011 Jan 18; 1542: 77-84.

**BACKGROUND:** Storytelling is emerging as a powerful tool for health promotion in vulnerable populations. However, these interventions remain largely untested in rigorous studies. **OBJECTIVE:** To test an interactive storytelling intervention involving DVDs. **DESIGN:** Randomized, controlled trial in which comparison patients received an attention control DVD. Separate random assignments were performed for patients with controlled or uncontrolled hypertension. (ClinicalTrials.gov registration number: NCT00875225). **SETTING:** An inner-city safety-net clinic in the southern United States. **PATIENTS:** 230 African Americans with hypertension. **INTERVENTION:** 3 DVDs that contained patient stories. Storytellers were drawn from the patient population. **MEASUREMENTS:** The outcomes were differential change in blood pressure for patients in the intervention versus the comparison group at baseline, 3 months, and 6 to 9 months.

**RESULTS:** 299 African American patients were randomly assigned between December 2007 and May 2008 and 76.9% were retained throughout the study. Most patients (71.4%) were women, and the mean age was 53.7 years. Baseline mean systolic and diastolic pressures were similar in both groups. Among patients with baseline uncontrolled hypertension, reduction favored the intervention group at 3 months for both systolic



(11.21 mm Hg [95% CI, 2.51 to 19.9 mm Hg];  $P = 0.012$ ) and diastolic (6.43 mm Hg [CI, 1.49 to 11.45 mm Hg];  $P = 0.012$ ) blood pressures. Patients with baseline controlled hypertension did not significantly differ over time between study groups. Blood pressure subsequently increased for both groups, but between-group differences remained relatively constant. **LIMITATION:** This was a single-site study with 23% loss to follow-up and only 6 months of follow-up.

**CONCLUSION:** The storytelling intervention produced substantial and significant improvements in blood pressure for patients with baseline uncontrolled hypertension. **PRIMARY FUNDING SOURCE:** Finding Answers: Disparities Research for Change, a national program of the Robert Wood Johnson Foundation.

**INSPIREHEALTH'S CONCLUSION:** Narrative storytelling interventions may also have a favourable impact on cancer outcomes.

## LUNG CANCER

Jeong, T-, B.-K Park, Y. -W Lee, et al.

### Prospective Analysis on Survival Outcomes of Non-Small Cell Lung Cancer Stages Over IIIb Treated with HangAm-Dan.

*Chinese Journal of Lung Cancer.* 2010 November 2010; 1311: 1009-1015.

**BACKGROUND AND OBJECTIVE:** Non-small cell lung cancer (NSCLC) stages over IIIb still remain as an intractable disease. Survival rate of NSCLC stages over IIIb could be increased through chemotherapy and radiation, but results are not satisfactory. Oriental medicine herbal formula, HangAm-Dan (HAD) has been developed for anti-tumor purpose and several previous studies have already reported its effects. The aim of this study is to assess HAD's efficacy on prolonging the survival rate of NSCLC stages over IIIb. **METHODS:** We have administered 3 000 mg of HAD daily to patients. The study included 74 first visit patients of East-West Cancer Center (EWCC) from November 2007 to April 2008, diagnosed with inoperable NSCLC stages over IIIb. Among them, 30 patients were in HAD group and 44 patients were in combined group with conventional therapy and HAD. We have observed and analyzed their overall survival.

**RESULTS:** Of total 74 patients, overall 1 year, 2 year survival rates and the median survival time were 62.1%, 34.9% and 17.0 months (95%CI: 12.9-21.1). NSCLC stage IIIb patients showed higher survival rates than NSCLC stage IV patients ( $P=0.408$ ). The 1 year, 2 year survival rates and the median survival time of the combined group were 70.5%, 37.9% and 20.0 months (95%CI: 16.4-24.6). In HAD group, the 1 year, 2 year survival rates and the median survival time were 50.0%, 25.7% and 12.0 months (95%CI: 6.6-17.4). The combined therapy group showed higher survival rates than the HAD group ( $P=0.034$ ). Each groups treated with HAD for more than 4 weeks showed higher survival rates than those treated for less than 4 weeks, but there was no significant difference ( $P=0.278$ ). In hazard ratio, the combined therapy group showed lower mortality rate than the HAD group with statistical significance ( $P=0.040$ ).

**CONCLUSION:** HAD could prolong the survival rate of inoperable NSCLC stages over IIIb. HAD is more effective when combined with conventional therapy. In the future, more controlled clinical trials with larger sample in multi-centers are needed to reevaluate the efficacy and safety of HAD.

## CANCER-RELATED ANOREXIA

Lee, JJ

### A Phase II Study of an Herbal Decoction that Includes Astragali Radix for Cancer-Associated Anorexia in Patients with Advanced Cancer.

*Integrative Cancer Therapies.* 2010 March 2010; 91: 24-31.

**HYPOTHESIS:** Anorexia and cancer cachexia produce significant loss of adipose tissue and muscle mass and eventually reduce survival in cancer patients. **STUDY DESIGN:** This phase II study was conducted to assess the efficacy and the safety of an herbal decoction with Astragali Radix in patients with anorexia in advanced cancer. **METHODS:** All patients with histologic evidence of an incurable malignancy had a weight loss of at least 5% during the preceding 6 months and a patient-estimated severe anorexia. The herbal decoction was administered 30 minutes after meals, three times a day for 3 weeks. The score of appetite, body weight, the cytokines, IL-1beta, IL-6, TNF-alpha, and anthropometric measurements were assessed. For the assessment of anorexia, a visual analog scale (VAS: 0 mm = no anorexia, 100 mm = maximal anorexia) was used.



**RESULTS:** Eleven patients were recruited from January, 2007 to January, 2009. The mean age was 59.8 years old. The change in anorexia from baseline with the herbal decoction was significantly different and anorexia was improved (anorexia VAS score, 60mm vs. 40mm,  $p = 0.008$ ). The mean value of the maximal body weight was 55.6 kg and differed significantly from the 54.6 kg at baseline ( $p = 0.009$ ). Changes in cytokine levels and anthropometric measurements from baseline to the 3rd week were not significant. All toxicities were manageable.

**CONCLUSION:** Appetite and body weight were improved with the herbal decoction. This herbal decoction shows some potential for management of cancer-related anorexia.

## STUDY OF THE MONTH

Engel, P, G. Fagherazzi, S. Mesrine, et al.

### Joint Effects of Dietary Vitamin D and Sun Exposure on Breast Cancer Risk: Results from the French E3N Cohort.

*Cancer Epidemiology Biomarkers and Prevention*. 2011 January 2011; 201: 187-195.

**BACKGROUND:** Ecological studies have suggested that vitamin D production through ultraviolet (UV) solar irradiance could reduce breast cancer (BC) risk. Although studies restricted to dietary vitamin D intake have provided inconsistent results, little is known about the relationship between pre- and postmenopausal BC and combined intakes from diet, supplements, and sun exposure. **METHODS:** Cox proportional hazards regression models evaluated the association between vitamin D intakes, mean daily ultraviolet radiation dose (UVRd) at the place of residence and risk of BC among 67,721 women of the French E3N cohort. All analyses were stratified on menopausal status taking into account important confounders including calcium consumption.

**RESULTS:** During 10 years of follow-up, a total of 2,871 BC cases were diagnosed. Dietary and supplemental vitamin D intakes were not associated with BC risk; however, in regions with the highest UVRd, postmenopausal women with high dietary or supplemental vitamin D intake had a significantly lower BC risk as compared with women with the lowest vitamin D intake (HR = 0.68, 95% CI: 0.54-0.85, and HR = 0.57, 95% CI: 0.36-0.90, respectively).

**CONCLUSION:** Our results suggest that a threshold of vitamin D exposure from both sun and diet is required to prevent BC and this threshold is particularly difficult to reach in postmenopausal women at northern latitudes where quality of sunlight is too poor for adequate vitamin D production.



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