



# REsearch UPDATES

FOR THE LATEST IN WORLDWIDE INTEGRATED CANCER CARE

## Inside

### CANCERS

Breast Cancer .....	1
Colorectal Cancer .....	3
Prostate Cancer .....	5
Melanoma .....	5

### THERAPIES

CAM use in Treatment .....	4
Nutrition .....	4

### STUDY OF THE MONTH .....

**IN THIS ISSUE:** This month's edition of InspireHealth's Research Updates features articles that report on how physical activity helps prevention or treatment of colorectal, prostate and BRCA1/2 positive breast cancers. Additional studies report on vitamin D (colorectal), nutrition (laryngeal), social stress (breast), and the attitudes about the use of CAM.

In our *Study of the Month*, Hwang and colleagues report that human papillomavirus (HPV)-positive women who had a diet low in fruits and vegetables were more likely to develop cervical cancer than HPV-positive women whose diet was higher in fruits and vegetables.

*Research Updates* is published once a month to provide the latest integrated cancer care research to patients, health care providers, and the public.

**To support this valuable educational service, please donate at:**  
[www.inspirehealth.ca/donate](http://www.inspirehealth.ca/donate)



**InspireHealth**  
 INTEGRATED CANCER CARE

[www.inspirehealth.ca](http://www.inspirehealth.ca)

## BREAST CANCER

Walker, EM, A. I. Rodriguez, B. Kohn, et al.

### Acupuncture Versus Venlafaxine for the Management of Vasomotor Symptoms in Patients with Hormone Receptor-Positive Breast Cancer: A Randomized Controlled Trial.

*Journal of Clinical Oncology*. 2010 Feb 1; 284: 634-640.

**PURPOSE:** Vasomotor symptoms are common adverse effects of antiestrogen hormone treatment in conventional breast cancer care. Hormone replacement therapy is contraindicated in patients with breast cancer. Venlafaxine (Effexor), the therapy of choice for these symptoms, has numerous adverse effects. Recent studies suggest acupuncture may be effective in reducing vasomotor symptoms in menopausal women. This randomized controlled trial tested whether acupuncture reduces vasomotor symptoms and produces fewer adverse effects than venlafaxine. **PATIENTS AND METHODS:** Fifty patients were randomly assigned to receive 12 weeks of acupuncture (n = 25) or venlafaxine (n = 25) treatment. Health outcomes were measured for up to 1 year post-treatment.

**RESULTS:** Both groups exhibited significant decreases in hot flashes, depressive symptoms, and other quality-of-life symptoms, including significant improvements in mental health from pre- to post-treatment. These changes were similar in both groups, indicating that acupuncture was as effective as venlafaxine. By 2 weeks post-treatment, the venlafaxine group experienced significant increases in hot flashes, whereas hot flashes in the acupuncture group remained at low levels. The venlafaxine group experienced 18 incidences of adverse effects (eg, nausea, dry mouth, dizziness, anxiety), whereas the acupuncture group experienced no negative adverse effects. Acupuncture had the additional benefit of increased sex drive in some women, and most reported an improvement in their energy, clarity of thought, and sense of well-being.

**CONCLUSION:** Acupuncture appears to be equivalent to drug therapy in these patients. It is a safe, effective and durable treatment for vasomotor symptoms secondary to long-term antiestrogen hormone use in patients with breast cancer.



Surtees, PG, N. W. J. Wainwright, R. N. Luben, K. -T Khaw and S. A. Bingham.

### **No Evidence that Social Stress is Associated with Breast Cancer Incidence.**

*Breast Cancer Res Treat.* 2010 February; 1201: 169-174.

Women commonly attribute the experience of stress as a contributory cause of breast cancer. The purpose of this study is to investigate the associations between a history of social stress and breast cancer risk. A total of 11,467 women with no prior history of breast cancer, participants in the European Prospective Investigation into Cancer (EPIC)-Norfolk population-based prospective cohort study, completed a comprehensive assessment of lifetime social adversity exposure. Summary measures of social adversity were defined according to difficult circumstances in childhood, stressful life events and longer-term difficulties in adulthood, derived measures representing the subjective 'impact' of life events and associated 'stress adaptive capacity', and perceived stress over a 10-year period. Incident breast cancers were identified through linkage with cancer registry data. During 102,514 (median 9) person-years of follow-up, 313 incident breast cancers were identified. No associations were observed between any of the summary social adversity measures and subsequent breast cancer risk, with or without adjustment for age, menopausal status, parity, use of menopausal hormones, age at menarche, age at first birth, family history of breast cancer, physical activity, social class, body mass index, height, and alcohol intake.

This study found no evidence that social stress exposure or individual differences in its experience are associated with the development of breast cancer. These findings may aid strategies designed to meet the psychosocial and emotional needs of breast cancer survivors and may be interpreted in a positive way in the context of commonly voiced beliefs that the experience of stress is a contributory cause of their disease.

---

Pijpe, A, P. Manders, R. M. Brohet, et al.

### **Physical Activity and the Risk of Breast Cancer in BRCA1/2 Mutation Carriers.**

*Breast Cancer Res Treat.* 2010 February; 1201: 235-244.

BRCA1/2 mutation carriers have a high lifetime risk of developing breast cancer. Differences in penetrance indicate that this risk may be influenced by lifestyle factors. Because physical activity is one of the few modifiable risk factors, it may provide a target to add to breast cancer prevention in this high-risk population. We examined the association between self-reported lifetime sports activity and breast cancer risk in a nationwide retrospective cohort study, including 725 carriers, of whom 218 had been diagnosed with breast cancer within 10 years prior to questionnaire completion.

#### **InspireHealth's two-day LIFE Program**

This unique life-changing cancer care program provides you with powerful tools to improve your recovery and survival.

In a supportive setting, you will learn about your body's innate healing capacity, the latest scientific research in integrative care, and the many ways you can benefit from natural approaches to healing.

**Call today to register:  
604-734-7125**

We found a nonsignificantly decreased risk for ever engaging in sports activity (HR = 0.84, 95%CI = 0.57-1.24). Among women who had participated in sports, a medium versus low level of intensity and duration (i.e., between 11.0 and 22.7 mean MET hours/week averaged over a lifetime) reduced the risk of breast cancer (HR = 0.59, 95%CI = 0.36-0.95); no dose-response trend was observed. For mean hours/week of sports activity, a nonsignificant trend was observed (HR<sub>low</sub> versus never = 0.93, 95%CI = 0.60-1.43; HR<sub>medium</sub> versus never = 0.81, 95%CI = 0.51-1.29; HR<sub>high</sub> versus never = 0.78, 95%CI = 0.48-1.29; p trend overall = 0.272; p trend active women = 0.487). For number of years of sports activity no significant associations were found. Among women active in sports before age 30, mean MET hours/week showed the strongest inverse association of all activity measures (HR<sub>medium</sub> versus low = 0.60, 95%CI = 0.38-0.96; HR<sub>high</sub> versus low = 0.58, 95%CI = 0.35-0.94; p trend = 0.053). Engaging in sports activity after age 30 was also inversely associated with breast cancer risk (HR = 0.63, 95%CI = 0.44-0.91).

Our results indicate that sports activity may reduce the risk of breast cancer in BRCA1/2 mutation carriers.

## COLORECTAL CANCER



Halle, M and M. H. Schoenberg.

### Physical Activity in the Prevention and Treatment of Colorectal Carcinoma

*Deutsches Arzteblatt International*. 2009 Oct; 10644: 722-727.

**BACKGROUND:** Colorectal carcinoma is the most common type of tumor in Western countries. The risk of developing colorectal carcinoma depends both on genetic factors (familial predisposition) and on lifestyle-related factors such as body-mass index, level of physical activity, and nutritional behavior. Regular physical activity is important in primary prevention, and there is also evidence that the prognosis after treatment of a colorectal carcinoma can be improved by exercise. **METHODS:** The PubMed database was searched for relevant articles that appeared in the last 10 years, and selected articles were evaluated.

**RESULTS:** Cross-sectional studies have shown that regular physical activity (ca. 7 hours of brisk walking per week) lowers the risk of colon carcinoma by 40%. Physical activity also improves the outcome of patients already diagnosed with colorectal carcinoma: for example, patients with advanced disease (UICC stage II or III) have been found to survive significantly longer if they perform 4 hours of brisk walking per week, or the equivalent degree of physical exercise.

**CONCLUSIONS:** Cross-sectional studies show that physically active persons are less likely to develop colorectal carcinoma than physically inactive persons, and that they have better outcomes in the event that they do develop the disease. The positive findings with respect to secondary prevention still need to be confirmed in interventional trials, but in primary prevention, at least, physical activity should be actively promoted, along with other beneficial lifestyle habits and screening measures.

Jenab, M, H. B. Bueno-de-Mesquita, P. Ferrari, et al.

### Association between Pre-Diagnostic Circulating Vitamin D Concentration and Risk of Colorectal Cancer in European Populations: A Nested Case-Control Study.

*BMJ*. 2010 340b5500.

**OBJECTIVE:** To examine the association between pre-diagnostic circulating vitamin D concentration, dietary intake of vitamin D and calcium, and the risk of colorectal cancer in European populations. **DESIGN:** Nested case-control study. **SETTING:** The study was conducted within the EPIC study, a cohort of more than 520 000 participants from 10 western European countries. **PARTICIPANTS:** 1248 cases of incident colorectal cancer, which developed after enrolment into the cohort, were matched to 1248 controls. **MAIN OUTCOME MEASURES:** Circulating vitamin D concentration (25-hydroxy-vitamin-D, 25-(OH)D) was measured by enzyme immunoassay. Dietary and lifestyle data were obtained from questionnaires. Incidence rate ratios and 95% confidence intervals for the risk of colorectal cancer by 25-(OH)D concentration and levels of dietary calcium and vitamin D intake were estimated from multivariate conditional logistic regression models, with adjustment for potential dietary and other confounders.

**RESULTS:** 25-(OH)D concentration showed a strong inverse linear dose-response association with risk of colorectal cancer ( $P$  for trend  $\text{or}=100.0 \text{ nmol/l}: 0.77 (0.56 \text{ to } 1.06)$ ). In analyses by quintile of 25-(OH)D concentration, patients in the highest quintile had a 40% lower risk of colorectal cancer than did those in the lowest quintile ( $P<0.001$ ). Subgroup analyses showed a strong association for colon but not rectal cancer ( $P$  for heterogeneity=0.048). Greater dietary intake of calcium was associated with a lower colorectal cancer risk. Dietary vitamin D was not associated with disease risk. Findings did not vary by sex and were not altered by corrections for season or month of blood donation.

**CONCLUSIONS:** The results of this large observational study indicate a strong inverse association between levels of pre-diagnostic 25-(OH)D concentration and risk of colorectal cancer in western European populations. Further randomized trials are needed to assess whether increases in circulating 25-(OH)D concentration can effectively decrease the risk of colorectal cancer.



## CAM USE IN CANCER TREATMENT

Schernhammer, ES, G. Haidinger, T. Waldhor and C. Vutuc.

### Attitudes about the use of Complementary and Alternative Medicine in Cancer Treatment.

*J Altern Complement Med.* 2009 Oct; 15(10): 1115-1120.

**OBJECTIVES:** The aim of this study was to achieve an understanding what determines the attitude of people toward complementary and alternative medicine (CAM) is essential in decisions about costly therapies in cancer treatment. **DESIGN:** This study involved population-based surveys conducted in 1995 and 2005. **SETTING:** In 1995 and 2005, a quota sample of 2400 Austrians ages  $>$  or  $=15$  was selected and invited in writing to participate in a survey to study beliefs and attitudes about cancer, its risk factors, and treatment. The sample comprised 0.04% of the population  $>$  or  $=15$  years of age and was representative in terms of age, sex, occupational status, and area of residence. **SUBJECTS:** The subjects included 4073 Austrian adults (2073 participants enrolled in the 1995 survey and 2000 participants of the 2005 survey). **INTERVENTION:** Respondents were visited in their homes by trained interviewers. The interview was face-to-face, using a standardized questionnaire. **OUTCOME MEASURES:** We used a dichotomized variable as the outcome, placing high value on CAM (rated as 1 or 2 on a 5-level Likert scale) versus everything else (rated 3-5).

**RESULTS:** Positive personal experiences with people cured of cancer improved the likelihood of a positive perception of CAM (odds ratio [OR], 1.36; 95% confidence interval [CI], 1.17-1.59 for those who reported knowing someone who was cured of cancer, compared to those who did not). In multivariate models adjusting for personal attitude toward mainstream medicine, subjects with more formal education were also more likely to believe that CAM is valuable (OR, 1.28; 95% CI, 1.02-1.61), as were women (OR, 1.40; 95% CI, 1.20-1.64) and people ages 70 and above (OR, 1.46; 95% CI, 1.02-2.08). A higher appreciation of mainstream medicine was inversely associated with the value placed on CAM in cancer therapy (OR, 0.43; 95% CI, 0.22-0.85).

**CONCLUSIONS:** In this, to our knowledge, the first study to evaluate predictors of CAM preference in cancer treatment in a national probability sample, we found more formal education, female gender, and older age to be the strongest predictors of a person favoring CAM therapy in cancer treatment. Our data also suggest that people who are satisfied with conventional care were less inclined to value CAM, whereas a positive personal experience with cancer cures improved positive perception of CAM.

## NUTRITION



Edefonti, V, F. Bravi, W. Garavello, et al.

### Nutrient-Based Dietary Patterns and Laryngeal Cancer: Evidence from an Exploratory Factor Analysis.

*Cancer Epidemiology Biomarkers and Prevention.* 2010 January; 19(1): 18-27.

**BACKGROUND:** The issue of diet and laryngeal cancer has been rarely addressed considering the potential role of dietary patterns. **METHODS:** We examined this association using data from a case-control study carried out between 1992 and 2000. Cases were 460 histologically confirmed incident laryngeal cancers hospitalized in two Italian areas. Controls were 1,088 subjects hospitalized for acute non-neoplastic diseases unrelated to tobacco or alcohol consumption. Dietary habits were investigated through a 78-item food frequency questionnaire. A posteriori dietary patterns were identified through principal component factor analysis carried out on a selected set of 28 major nutrients. The internal reproducibility, robustness, and reliability of the identified patterns were evaluated. Odds ratios (OR) of laryngeal cancer and 95% confidence intervals (95% CI) were estimated using unconditional multiple logistic regression models on quartiles of factor scores.



**RESULTS:** We identified five major dietary patterns named "animal products," "starch-rich," "vitamins and fiber," "vegetable unsaturated fatty acids," and "animal unsaturated fatty acids." The vitamins and fiber dietary pattern was inversely associated with laryngeal cancer (OR, 0.35; 95% CI, 0.24-0.52 for the highest versus the lowest score quartile), whereas the animal products (OR, 2.34; 95% CI, 1.59-3.45) and the animal unsaturated fatty acids (OR, 2.07; 95% CI, 1.42-3.01) patterns were directly associated with it. There was no significant association between the vegetable unsaturated fatty acids and the starch-rich patterns and laryngeal cancer risk.

**CONCLUSION:** These findings suggest that diets rich in animal products and animal fats are directly related, and those rich in fruit and vegetables inversely related, to laryngeal cancer risk

## PROSTATE CANCER

Antonelli, JA, L. W. Jones, L. L. Banez, et al.

### Exercise and Prostate Cancer Risk in a Cohort of Veterans Undergoing Prostate Needle Biopsy.

*J Urol.* 2009 November; 182(5): 2226-2231.

**PURPOSE:** Epidemiological and molecular evidence suggest potential associations between exercise and prostate cancer risk reduction. We further characterized this relationship by examining exercise and cancer risk among men undergoing prostate needle biopsy. **MATERIALS AND METHODS:** A total of 190 men who underwent prostate biopsy at the Durham Veterans Affairs Medical Center completed a questionnaire on current exercise behavior. Participants were asked average frequency of mild, moderate and strenuous intensity exercise in a typical week, as well as average duration as assessed by the Godin Leisure Time Exercise Questionnaire. Total current exercise was calculated in terms of metabolic equivalent task hours per week. Primary outcome measures were prostate biopsy result and Gleason sum.

**RESULTS:** After adjusting for age, race, body mass index, prostate specific antigen, digital rectal examination, family history, previous prostate biopsy and comorbidity score, men who reported 9 or more metabolic equivalent task hours per week of exercise were significantly less likely to have cancer on biopsy (OR 0.35, CI 0.17-0.75,  $p = 0.007$ ). Furthermore, among men with malignant biopsy results, reporting moderate exercise (3 to 8.9 metabolic equivalent task hours weekly) was associated with a lower risk of high grade disease (Gleason 7 or greater, OR 0.14, CI 0.02-0.94,  $p = 0.04$ ).

**CONCLUSIONS:** To our knowledge these results provide the first evidence of an association between exercise and prostate cancer risk as well as grade at diagnosis in men scheduled to undergo prostate biopsy. Specifically moderate exercise was associated with a lower risk of prostate cancer and in men with cancer, lower grade disease. Further investigation using an objective measure of exercise in a larger sample size is required to confirm these findings.

## MELANOMA

Veierod, MB, H. -O Adami, E. Lund, B. K. Armstrong and E. Weiderpass.

### Sun and Solarium Exposure and Melanoma Risk: Effects of Age, Pigmentary Characteristics, and Nevi.

*Cancer Epidemiology Biomarkers and Prevention.* 2010 January; 19(1): 111-120.

**BACKGROUND:** Few prospective studies have analyzed solar and artificial (solarium) UV exposure and melanoma risk. We investigated these associations in a Norwegian-Swedish cohort study and addressed effect modification by age, pigmentary characteristics, and nevi. **METHODS:** The cohort included women ages 30 to 50 years at enrollment from 1991 to 1992. Host factors and exposure to sun and solariums in life decades were collected by questionnaire at enrollment. Relative risks (RR) with 95% confidence intervals (CI) were estimated by Poisson regression.





**RESULTS:** Among 106,366 women with complete follow-up through 2005, 412 melanoma cases were diagnosed. Hair color and large, asymmetric nevi on the legs were strongly associated with melanoma risk (Ptrend [less-than or equal to] 0.001), and the RR for [greater-than or equal to]2 nevi increased from brown/black to blond/yellow to red-haired women (RRs, 1.72, 3.30, and 4.95, respectively; P interaction = 0.18). Melanoma risk increased significantly with the number of sunburns and bathing vacations in the first three age decades ( P trend [less-than or equal to] 0.04) and solarium use at ages 30 to 39 and 40 to 49 years [RRs for solarium use [greater-than or equal to]1 time/mo 1.49 (95% CI, 1.11-2.00) and 1.61 (95% CI 1.10-2.35), respectively; Ptrend [less-than or equal to] 0.02]. Risk of melanoma associated with sunburns, bathing vacations, and solarium use increased with accumulating exposure across additional decades of life.

**CONCLUSIONS:** Melanoma risk seems to continue to increase with accumulating intermittent sun exposure and solarium use in early adulthood. Apparently, super-multiplicative joint effects of nevi and hair color identify people with red hair and multiple nevi as a very high risk group and suggest important gene-gene interactions involving MC1R in melanoma etiology.

## STUDY OF THE MONTH

Hwang, JH, J. K. Lee, T. J. Kim and M. K. Kim.

### The Association between Fruit and Vegetable Consumption and HPV Viral Load in High-Risk HPV-Positive Women with Cervical Intraepithelial Neoplasia.

*Cancer Causes and Control.* 2010 January; 211: 51-59.

We evaluated the relationship between the dietary intake of vegetables and fruits, and the risk of cervical intraepithelial neoplasia (CIN) and determined whether these associations were modified by human papillomavirus (HPV) viral load. We enrolled 1,096 women aged 18-65 to participate in a HPV cohort study from March 2006 up to present. For this analysis, we included 328 HPV-positive women (166 controls, 90 CIN I and 72 CIN II/III). The multivariate odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were estimated by multinomial logistic methods.

After controlling for potential confounders, we found that a higher HPV viral load was associated with an increased risk of CIN I (OR = 2.68, 95% CI, 1.19-6.04) and CIN II/III (OR = 2.78, 95% CI, 1.15-6.72). The relationships between HPV infection, dietary intake of vegetables and fruits and risk of CIN were not statistically significant. However, subjects with lower intake of vegetables and fruits, and a higher viral load ([greater-than or equal to]15.5) have a higher risk of CIN II/III (OR = 2.84(1.26-6.42), interaction p = 0.06 for vegetables; OR = 2.93(1.25-6.87), interaction p = 0.01 for fruits), compared with subjects with lower intake of vegetables and fruits, and a lower viral load (<15.5).

Our findings suggest that the dietary intake of vegetables and fruits is associated with the progression of cervical carcinogenesis.

InspireHealth provides patients with the knowledge, tools, and services to support their overall health during and after cancer treatment.

Our medical doctors value conventional cancer treatments such as chemotherapy, radiation, and surgery. At the same time, they recognize the importance of supporting health, immune function, body, mind, and spirit.

InspireHealth's programs are supported by current research and can be safely integrated with patient's conventional treatments.

InspireHealth's *Research Updates* are compiled by Jan Rennie and Dr. Julius Halaschek-Wiener, PhD—with guidance from the editorial board—using InspireHealth's *Research Information System*, a unique integrated cancer care knowledge management database. The editorial team selects authoritative articles based on their evidence and their relevance to this area of medicine.

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 Dr. Julius Halaschek-Wiener, PhD.

For more information, email [library@inspirehealth.ca](mailto:library@inspirehealth.ca)

