



# REsearch UPDATES

FOR THE LATEST IN WORLDWIDE INTEGRATED CANCER CARE

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**IN THIS ISSUE:** Lebret and colleagues found that written guidance on diet and exercise was helpful for prostate cancer patients. Nakaya and associates found that men whose partner had breast cancer were at an increased risk for depression requiring hospitalization. Nechuta et al. found that vitamin supplement use within the first six months of diagnosis of breast cancer reduced the risk of mortality and recurrence. Liu and associates found that educating early stage breast cancer patients about the reality of risk of recurrence helped to alleviate anxiety. Collinge and colleagues found that using a DVD to learn about basic massage techniques enhanced family caregivers' sense of self-efficacy and increased patient comfort, which improved the quality of the relationships between the caregivers and patients. In our study of the month, Schmitz et al. found that a program of slowly progressive weight lifting did not increase the incidence of lymphedema in a group at risk.

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## PROSTATE CANCER



Lebret, T, P. Coloby, J. L. Descotes, et al.

### Educational Tool-Kit on Diet and Exercise: Survey of Prostate Cancer Patients about to Receive Androgen Deprivation Therapy.

*Urology*. 2010 Dec; 766: 1434-1439.

**OBJECTIVES:** To test a tool-kit designed to improve well-being in patients with prostate cancer. Lifestyle changes might lessen the metabolic, cardiovascular, and osseous side effects of androgen deprivation therapy (ADT) in prostate cancer patients. **METHODS:** Urologists supplied 10 consecutive patients initiating ADT with a tool-kit (information brochure, practical guidance on diet and exercise, recipe booklet, and lifestyle diary). The urologists completed a total 4 questionnaires; at study initiation, one at the patients' first and second visits, and one at study completion

**RESULTS:** Overall, 91 urologists completed all questionnaires; 585 patients (median age, 75 years) were seen at the first visit, and 511 patients at the second. Patient response rate to the first questionnaire was 62% and 56% to the second. After the first visit, 82% of respondents reported being very glad or glad to receive the kit; among those having read the practical guidance (301/362), 57% had started implementation and 36% intended to do so. After the second visit, 76% were satisfied with the tool-kit and 84% were implementing guidance. Clinician satisfaction rate was 82%: benefits were improved patient dialogue (62%), follow-up (55%), and better explanation of side effects (51%). Only 14 clinicians were not pleased by the tool kit. Their main criticisms (too long, tedious, not tailored to individual needs) matched those of patients.

**CONCLUSIONS:** Written detailed guidance on diet and physical exercise for patients about to receive ADT met a genuine need and was well perceived by both clinicians and patients. Implementation rate was high. However, content should be adapted to patient age and disease stage.



## BREAST CANCER

Nakaya, N, K. Saito-Nakaya, P. E. Bidstrup, et al.

### Increased Risk of Severe Depression in Male Partners of Women with Breast Cancer.

*Cancer*. 2010 01 Dec; 11623: 5527-5534.

**BACKGROUND:** A few small studies published to date have suggested that major psychosocial problems develop in the partners of cancer patients; however, to the authors' knowledge, no studies to date have addressed their risk for severe depression. In a retrospective cohort study, the risk for hospitalization with an affective disorder of the male partners of women with breast cancer was investigated, using unbiased, nationwide, population-based information. **METHODS:** Followed were 1,162,596 men born between 1925 and 1973 who were aged  $\geq 30$  years at study entry, resided in Denmark between 1994 and 2006, had no history of hospitalization for an affective disorder, and had lived continuously with the same partner for at least 5 years. A Cox regression analysis included detailed clinical information regarding the diagnosis and treatment of breast cancer and on annually updated socioeconomic and health-related indicators obtained from national administrative and disease registers.

**RESULTS:** During the 13 years of follow-up, breast cancer was diagnosed in the partners of 20,538 men. On multivariable analysis, men whose partner was diagnosed with breast cancer were found to be at an increased risk of being hospitalized with an affective disorder (hazards ratio, 1.39; 95% confidence interval, 1.20-1.61), with a dose-response pattern for the severity of breast cancer. Furthermore, men whose partner died after breast cancer had a significant, 3.6-fold increase in risk for an affective disorder when compared with men whose partner survived breast cancer.

**CONCLUSIONS:** The results of the current study supported the hypothesis that men whose partner had breast cancer were at an increased risk for hospitalization with an affective disorder. This cohort study supported the hypothesis that the male partners of women with breast cancer are at a significantly increased risk for hospitalization with affective disorders. Results concluded that a diagnosis of breast cancer not only affects the life of the patient but may also seriously affect their partner.

Nechuta S, Lu W, Chen Z, et al.

### Vitamin Supplement use during Breast Cancer Treatment and Survival: A Prospective Cohort Study.

*Cancer Epidemiol Biomarkers Prev*. 2010 Dec 21;

**BACKGROUND:** Antioxidants may protect normal cells from the oxidative damage that occurs during radiotherapy and certain chemotherapy regimens, however, the same mechanism could protect tumor cells and potentially reduce effectiveness of cancer treatments. We evaluated the association of vitamin supplement use in the first six-months after breast cancer diagnosis and during cancer treatment with total mortality and recurrence. **METHODS:** We conducted a population-based prospective cohort study of 4,877 women aged 20-75 years diagnosed with invasive breast cancer in Shanghai, China between March 2002 and April 2006. Women were interviewed approximately six-months after diagnosis and followed-up by in-person interviews and record linkage with the vital statistics registry.

**RESULTS:** During a mean follow-up of 4.1 years, 444 deaths and 532 recurrences occurred. Vitamin use shortly after breast cancer diagnosis was associated with reduced mortality and recurrence risk, adjusted for multiple lifestyle factors, sociodemographics, and known clinical prognostic factors. Women who used antioxidants (vitamin E, vitamin C, multivitamins) had 18% reduced mortality risk (hazard ratio (HR) = 0.82, 95% confidence interval (CI): 0.65-1.02) and 22% reduced recurrence risk (HR = 0.78, 95% CI: 0.63-0.95). The inverse association was found regardless of whether vitamin use was concurrent or non-concurrent with chemotherapy, but was only present among patients who did not receive radiotherapy.

**CONCLUSIONS:** Vitamin supplement use in the first six months after breast cancer diagnosis may be associated with reduced risk of mortality and recurrence. **IMPACT:** Our results do not support the current recommendation that breast cancer patients should avoid use of vitamin supplements.



Chen, J, Q. Lv, M. Yu, X. et al.

### Randomized Clinical Trial of Chinese Herbal Medications to Reduce Wound Complications After Mastectomy for Breast Carcinoma.

*Br J Surg.* 2010 Dec; 97(12): 1798-1804.

**BACKGROUND:** Ischaemia and necrosis of skin flaps is a common complication after mastectomy. This study evaluated the influence of anisodamine and *Salvia miltiorrhiza* on wound complications after mastectomy for breast cancer. **METHODS:** Ninety patients undergoing mastectomy for breast carcinoma were divided into three groups. Group 1 received routine wound care, group 2 received intravenous *Salvia miltiorrhiza* after surgery for 3 days and group 3 similarly received intravenous anisodamine. Skin flaps were observed on postoperative days 4 and 8; areas of wound ischaemia and necrosis were graded and adverse events recorded.

**RESULTS:** There was no difference in demographic characteristics between the groups. At 4 days after surgery the rate of ischaemia and necrosis in groups 2 and 3 was significantly reduced compared with that in control group 1 (median wound score 680 versus 2338,  $P = 0002$ , and 376 versus 2338,  $P < 0001$ , respectively). This improvement in groups 2 and 3 continued to postoperative day 8 (both  $P < 0001$ ), but wound scores at this stage were better in group 3 than in group 2 (182 versus 692 respectively;  $P = 0022$ ). The volume of wound drainage was lower in group 3 than in group 1 ( $P = 0004$ ). The incidence of adverse effects was highest in group 3, and two patients in this group discontinued treatment. No significant complications were noted in group 2.

**CONCLUSION:** Anisodamine and *S. miltiorrhiza* were both effective in reducing skin flap ischaemia and necrosis after mastectomy, although anisodamine was associated with a higher rate of adverse effects.

Liu, Y, M. Perez, M. Schootman, et al.

### A Longitudinal Study of Factors Associated with Perceived Risk of Recurrence in Women with Ductal Carcinoma in Situ and Early-Stage Invasive Breast Cancer.

*Breast Cancer Res Treat.* 2010 Dec; 124(3): 835-844.

**BACKGROUND:** Breast cancer patients' perceived risk of recurrence has been associated with psychological distress. Little is known about the change of patients' perceived risk of recurrence over time and factors associated with their recurrence-risk perceptions. **METHODS:** We prospectively recruited 549 newly diagnosed early-stage breast cancer patients; patients completed interviews at 6 weeks, 6 months, 1 year, and 2 years after definitive surgical treatment. A random-effects regression model with repeated ordinal measurements was used to estimate the relationship between perceived risk of recurrence and demographic, medical, and psychosocial factors.

**RESULTS:** We analyzed data from 535 patients [34% ductal carcinoma in situ (DCIS); 20% non-white] who reported their perceived risk at one or more interviews. At the first interview, 16% reported having no lifetime risk of recurrence, and another 16% reported  $\geq 50\%$  risk of recurrence, including 15% of DCIS patients. Patients who were white ( $OR = 5.88$ , 95% CI 3.39-10.19) and had greater state anxiety ( $OR = 1.04$ , 95% CI 1.02-1.07) were more likely, while patients who received radiotherapy ( $OR = 0.72$ , 95% CI 0.54-0.96) and had more social support ( $OR = 0.59$ , 95% CI 0.46-0.75) were less likely to report higher risk of recurrence. Cancer stage was not significantly associated with perceived risk of recurrence. Perceived risk of recurrence did not change significantly over time.

**CONCLUSION:** Educating early-stage breast cancer patients about their actual risk could result in more realistic recurrence-risk perceptions, and increasing social support could help alleviate anxiety associated with exaggerated risk perceptions.

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## MASSAGE

Collinge, W, J. Kahn, T. Walton et al.

### Randomized Controlled Trial of Family Caregiver use of Massage as Supportive Cancer Care Following Multimedia Instruction.

*Journal of the Society for Integrative Oncology*. 2009

**PURPOSE:** Massage is one of the most effective forms of supportive care in cancer, but access to professional practitioners is limited for most patients. This abstract presents findings from an NCI sponsored randomized controlled trial (RCT) of family caregivers using simple techniques of touch and massage as supportive care guided by a home-based multimedia instructional program. The project assessed effects on (1) patient symptoms and side effects, (2) patient quality of life, and (3) caregiver attitudes toward use of touch as a form of caregiving. **METHOD:** A community-based, multiethnic sample of 97 adult caregiver-patient dyads was randomized to experimental or attention control conditions for 4 weeks. The sample consisted of 63 white, 13 black, 10 Chinese, 8 Hispanic, and 3 mixed-ethnicity dyads. Twenty-three types of cancer and all stages were represented. All data collection and instructional materials were produced in English, Spanish, and Chinese language versions. Instruction was provided in a 78-minute DVD featuring instruction by two oncology massage therapy researchers (J.K., T.W.), filmed in a workshop context with 11 patient-caregiver dyads (white, black, Hispanic, and Asian) learning and practicing the techniques. Content addressed communication, safety precautions related to cancer (lymphedema, etc.), manual techniques for comfort and relaxation, acupressure, simple light touch/holding for comfort, and positioning on home furniture. A 70-page illustrated manual accompanied the DVD. Experimental dyads were instructed to view the materials as often as they wished and practice techniques of their choice at least three times per week. Control caregivers were instructed to read to the patient from literature of the patient's choice at least three times per week. Both groups recorded "session effects" on one 20-minute "reporting session" per week, using 5 x 8 inch cards. Patients completed a two-sided card that reported pre- and 15 minutes postsession ratings of severity levels (10-point scale) for pain, fatigue, stress/anxiety, nausea, depression, and an optional "other." Safety monitoring for massage dyads was conducted by home visit observation by an oncology massage therapist. At baseline and 4-week follow-up, subjects also completed survey instruments assessing quality of life, stress, and caregiver attitudes. After the RCT, both groups were merged into the massage condition for a longitudinal study of utilization and effects over 20 weeks (longitudinal data to be reported separately).

**RESULTS:** Session data showed significant reductions for all symptoms after both activities. Reductions after reading ranged from 12 to 28%, and after massage, 29 to 44%, as follows: pain, 18% vs 34%; fatigue, 20% vs 32%; stress/ anxiety, 28% vs 44%; nausea, 12% vs 29%; depression, 22% vs 31; other, 17% vs 42%. Massage was significantly superior to reading for stress/anxiety ( $p < .01$ ), pain ( $p = .04$ ), fatigue ( $p = .01$ ), and other ( $p < .01$ ). Caregivers in the massage condition showed significant gains in their confidence and comfort with using touch and massage as forms of caregiving.

**CONCLUSION:** A multimedia instructional program in massage as supportive care at home offers family members a viable means of enhancing self-efficacy and satisfaction in caregiving. Family members can learn and apply safe and simple methods that increase patient comfort, reduce distress, and improve the quality of relationships.

## COLORECTAL CANCER

Fung, TT, F. B. Hu, K. Wu, et al.

### The Mediterranean and Dietary Approaches to Stop Hypertension (DASH) Diets and Colorectal Cancer.

*Am J Clin Nutr*. 2010 Dec; 92(6): 1429-1435.

**BACKGROUND:** Although the Mediterranean diet has been studied for cancer mortality and the Dietary Approaches to Stop Hypertension (DASH) diet shares similarities with the Mediterranean diet, few studies have specifically examined these 2 diets and incident colorectal cancer. **OBJECTIVE:** The objective was to prospectively assess the association between the Alternate Mediterranean Diet (aMed) and the DASH-style diet scores and risk of colorectal cancer in middle-aged men and women. **DESIGN:** A total of 87,256 women and 45,490 men (age 30-55 y for women and 40-75 y for men at baseline) without a history of cancer were



followed for  $\leq 26$  y. The aMed and DASH scores were calculated for each participant by using dietary information that was assessed  $\leq 7$  times during follow-up. Relative risks (RRs) for colorectal cancer were computed with adjustment for potential confounders.

**RESULTS:** We documented 1432 cases of incident colorectal cancer among women and 1032 cases in men. Comparing top with bottom quintiles of the DASH score, the pooled RR for total colorectal cancer was 0.80 (95% CI: 0.70, 0.91; P for trend = 0.0001). The corresponding RR for DASH score and colon cancer was 0.81 (95% CI: 0.69, 0.95; P for trend = 0.002). There was a suggestion of an inverse association with rectal cancer with a pooled RR of 0.73 (95% CI: 0.55, 0.98; P for trend = 0.31) when comparing top with bottom quintiles of DASH score. No association was observed with aMed score.

**CONCLUSION:** Adherence to the DASH diet (which involves higher intakes of whole grains, fruit, and vegetables; moderate amounts of low-fat dairy; and lower amounts of red or processed meats, desserts, and sweetened beverages) was associated with a lower risk of colorectal cancer.

## MULTIPLE CANCERS

Koutros, S, M. C. R. Alavanja, J. H. Lubin, et al.

### An Update of Cancer Incidence in the Agricultural Health Study.

*Journal of Occupational and Environmental Medicine.* 2010 Nov; 5211: 1098-1105.

**OBJECTIVE:** Our objective is to reevaluate cancer incidence among Agricultural Health Study participants.

**METHODS:** Standardized incidence ratios (SIRs) and relative standardized ratios were calculated.

**RESULTS:** A significant excess of prostate cancer was seen for private and commercial applicators (SIR = 1.19, 95% CI 1.14, 1.25 and SIR = 1.28, 95% CI = 1.00, 1.61, respectively). Excesses were observed for lip cancer (SIR = 1.97, 95% CI = 1.02, 3.44) and multiple myeloma (SIR = 1.42, 95% CI = 1.00, 1.95) among private applicators from North Carolina and for marginal zone lymphoma among Iowa spouses (SIR = 2.34, 95% CI = 1.21, 4.09).

**CONCLUSIONS:** Although lower rates of smoking and increased physical activity probably contribute to the lower overall cancer incidence, agricultural exposures including pesticides, viruses, bacteria, sunlight, and other chemicals may increase risks for specific cancer sites.

## SPIRITUALITY

Mao, JJ, P. F. Cronholm, E. Stein, et al.

### Positive Changes, Increased Spiritual Importance, and Complementary and Alternative Medicine (CAM) use among Cancer Survivors.

*Integrative Cancer Therapies.* 2010 Dec; 94: 339-347.

**PURPOSE:** Spirituality is an important component of the cancer experience. This study aims to assess characteristics of spiritual health following a cancer diagnosis, and evaluate the relationship between spiritual change and the use of complementary and alternative medicine (CAM) among a population-based cohort of cancer survivors. **METHOD:** A mailed, cross-sectional survey was completed by 614 cancer survivors identified through the Pennsylvania Cancer Registry. All subjects were 3 to 4.5 years postdiagnosis. Relationships between various characteristics of spiritual health and CAM use were examined, along with clinical and sociodemographic factors.

**RESULTS:** Although large proportions of individuals reported that having cancer had positively affected their spiritual well-being (e.g., 40.3% experienced highly positive spiritual changes, 68% felt a high sense of purpose, 75.9% reported being very hopeful), some individuals experienced negative spiritual change (36.1%) and continued to experience high levels of uncertainty (27.2%). In multivariate analyses, those survivors who felt spiritual life became more important (adjusted odds ratio [AOR] = 1.92, 95% confidence interval (CI) = 1.21-3.04, P = .006), or experienced positive changes resulting from the cancer experience (AOR = 1.99, 95% CI = 1.26-3.15, P = .003), were more likely to use CAM than those who stated otherwise.

**CONCLUSIONS:** Having cancer affects many different aspects of spiritual well-being, both positively and negatively. Positive changes and increased spiritual importance appear to be associated with the use of



CAM. Prospective research is needed to test whether integrating CAM into conventional cancer care systems will facilitate positive, spiritually transformative processes among diverse groups of cancer survivors.

## STUDY OF THE MONTH

Schmitz KH, Ahmed RL, Troxel AB, et al.

### Weight Lifting for Women at Risk for Breast Cancer-Related Lymphedema: A Randomized Trial.

*JAMA*. 2010 Dec 22; 304(24): 2699-2705.

**CONTEXT:** Clinical guidelines for breast cancer survivors without lymphedema advise against upper body exercise, preventing them from obtaining established health benefits of weight lifting. **OBJECTIVE:** To evaluate lymphedema onset after a 1-year weight lifting intervention vs. no exercise (control) among survivors at risk for breast cancer-related lymphedema (BCRL). **DESIGN, SETTING, AND PARTICIPANTS:** A randomized controlled equivalence trial (Physical Activity and Lymphedema trial) in the Philadelphia metropolitan area of 154 breast cancer survivors 1 to 5 years postunilateral breast cancer, with at least 2 lymph nodes removed and without clinical signs of BCRL at study entry. Participants were recruited between October 1, 2005, and February 2007, with data collection ending in August 2008. **INTERVENTION:** Weight lifting intervention included a gym membership and 13 weeks of supervised instruction, with the remaining 9 months unsupervised, vs. no exercise. **MAIN OUTCOME MEASURES:** Incident BCRL determined by increased arm swelling during 12 months ( $\geq 5\%$  increase in interlimb difference). Clinician-defined BCRL onset was also evaluated. Equivalence margin was defined as doubling of lymphedema incidence.

**RESULTS:** A total of 134 participants completed follow-up measures at 1 year. The proportion of women who experienced incident BCRL onset was 11% (8 of 72) in the weight lifting intervention group and 17% (13 of 75) in the control group (cumulative incidence difference [CID], -6.0%; 95% confidence interval [CI], -17.2% to 5.2%; P for equivalence = .04). Among women with 5 or more lymph nodes removed, the proportion who experienced incident BCRL onset was 7% (3 of 45) in the weight lifting intervention group and 22% (11 of 49) in the control group (CID, -15.0%; 95% CI, -18.6% to -11.4%; P for equivalence = .003). Clinician-defined BCRL onset occurred in 1 woman in the weight lifting intervention group and 3 women in the control group (1.5% vs. 4.4%, P for equivalence = .12).

**CONCLUSION:** In breast cancer survivors at risk for lymphedema, a program of slowly progressive weight lifting compared with no exercise did not result in increased incidence of lymphedema.

**TRIAL REGISTRATION:** [clinicaltrials.gov](http://clinicaltrials.gov) Identifier: NCT00194363.



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