



RESEARCH UPDATES

For the latest in worldwide integrated cancer care

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InspireHealth
INTEGRATED CANCER CARE

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Research Updates is produced once a month by InspireHealth to inform those interested of newly published articles in integrative cancer care. Authoritative articles are selected based on their evidence and their relevance to this area of medicine.

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Breast

Andersen, BL, H. -C Yang, W. B. Farrar, et al. **Psychologic Intervention Improves Survival for Breast Cancer Patients: A Randomized Clinical Trial.** *Cancer.* 2008 15 Dec; 11312: 3450-3458.

BACKGROUND. The question of whether stress poses a risk for cancer progression has been difficult to answer. A randomized clinical trial tested the hypothesis that cancer patients coping with their recent diagnosis but receiving a psychologic intervention would have improved survival compared with patients who were only assessed. **METHODS.** A total of 227 patients who were surgically treated for regional breast cancer participated. Before beginning adjuvant cancer therapies, patients were assessed with psychologic and behavioral measures and had a health evaluation, and a 60-mL blood sample was drawn. Patients were randomized to Psychologic Intervention plus assessment or Assessment only study arms. The intervention was psychologist led; conducted in small groups; and included strategies to reduce stress, improve mood, alter health behaviors, and maintain adherence to cancer treatment and care. Earlier articles demonstrated that, compared with the Assessment arm, the Intervention arm improved across all of the latter secondary outcomes. Immunity was also enhanced. **RESULTS.** After a median of 11 years of follow-up, disease recurrence was reported to occur in 62 of 212 (29%) women and death was reported for 54 of 227 (24%) women. Using Cox proportional hazards analysis, multivariate comparison of survival was conducted. As predicted, patients in the Intervention arm were found to have a reduced risk of breast cancer recurrence (hazards ratio [HR] of 0.55; $P = .034$) and death from breast cancer (HR of 0.44; $P = .016$) compared with patients in the Assessment only arm. Follow-up analyses also demonstrated that Intervention patients had a reduced risk of death from all causes (HR of 0.51; $P = .028$). **CONCLUSIONS.** Psychologic interventions as delivered and studied here can improve survival. copyright 2008 American Cancer Society.

Wayne, S, M. L. Neuhouser, C. M. Ulrich, et al. **Association between Alcohol Intake and Serum Sex Hormones and Peptides Differs by Tamoxifen use in Breast Cancer Survivors.** *Cancer Epidemiology Biomarkers*

and Prevention. 2008 November; 1711: 3224-3232.

Objective: To measure the association between alcohol intake and 11 hormones and peptides in postmenopausal breast cancer survivors and to evaluate whether this association differs by tamoxifen use. **Methods:** Self-reported alcohol intake was assessed via food frequency questionnaire on average 30 months post-breast cancer diagnosis in 490 postmenopausal women from three western states. Concurrently, a fasting blood sample was obtained for assay of estrone, estradiol, free estradiol, testosterone, free testosterone, dehydroepiandrosterone sulfate (DHEAS), sex hormone-binding globulin (SHBG), leptin, C-peptide, insulin-like growth factor-I (IGF-I), and IGF-binding protein-3. Adjusted means of these hormones and peptides were calculated for categories of alcohol intake, overall and stratified by tamoxifen use. **Results:** The association between alcohol intake and serum hormone and peptide levels differed by tamoxifen use. We found statistically significant inverse associations between alcohol intake and both leptin and SHBG values but only among tamoxifen users. In women not using tamoxifen, we found a positive association between alcohol intake and DHEAS but no association in tamoxifen users. **Conclusion:** Tamoxifen may modify the association between alcohol intake and serum hormones and peptides. The significant associations found for DHEAS and SHBG are in a direction considered unfavorable for breast cancer prognosis. Postmenopausal breast cancer survivors may benefit from decreasing their alcohol intake. Copyright copyright 2008 American Association for Cancer Research.

Wu, AH, G. Ursin, W. -P Koh, et al. **Green Tea, Soy, and Mammographic Density in Singapore Chinese Women.** *Cancer Epidemiology Biomarkers and Prevention.* 2008 December; 1712: 3358-3365. There is increasing evidence from observational studies that breast cancer risk is inversely associated with soy and green tea consumption. We investigated the effects of these two dietary agents on mammographic density, a well-established biomarker for breast cancer risk, in a cross-sectional analysis of mammograms and validated food frequency questionnaires from 3,315 Chinese women in Singapore. Percent mammographic density

(PMD) was assessed using a reproducible computer-assisted method. We used generalized linear models to estimate PMD by intake of soy, green tea, and black tea while adjusting for potential confounders. Daily green tea drinkers showed statistically significantly lower PMD (19.5%) than non-tea drinkers (21.7%; $P = 0.002$) after adjusting for relevant covariates. This difference in PMD between daily green tea drinkers and non-tea drinkers remained statistically significant after adjustment for soy ($P = 0.002$); the effect was more apparent among lower soy consumers (Q1-Q3; 21.9% versus 19.4%; $P = 0.002$) than in higher (Q4) consumers (20.9% versus 19.5%; $P = 0.32$). Black tea intake was unrelated to PMD. Only among postmenopausal women who reported very high soy intake (Q4) compared with those with less soy intake was there any association noted between PMD and soy intake (18.9% versus 20.5%; $P = 0.035$). Following adjustment for green tea intake, the association between soy and PMD was no longer statistically significant ($P = 0.52$). Our findings suggest that both regular green tea and high soy intake may have beneficial effects on the breast; the effect of green tea on PMD may be stronger than the effect of soy. Copyright copyright 2008 American Association for Cancer Research.

Prostate


Carmody, J, B. Olendzki, G. Reed, V. Andersen and P. Rosenzweig. **A Dietary Intervention for Recurrent Prostate Cancer After Definitive Primary Treatment: Results of a Randomized Pilot Trial.** *Urology.* 2008 December; 726: 1324-1328.

Objectives: Considerable evidence has shown that diet can affect both the incidence and the progression of prostate cancer. The objective of this study was to determine whether men in this situation could make a change to a diet emphasizing plant-based foods and fish and to examine the effect on quality of life (QOL) and prostate-specific antigen (PSA) velocity. **Methods:** A total of 36 men and their partners were randomly assigned to attend a series of 11 dietary and cooking classes that also integrated mindfulness practice as a support in making the change or a wait-list control group. Assessments were made of dietary intake, QOL, and PSA at baseline, after intervention (11 weeks), and 3 months after intervention. **Results:** The intervention group showed significant reductions in the consumption of saturated fat and increased consumption of vegetable proteins with accompanying reductions in animal proteins, including dairy products. They also showed increased QOL. Although no significant change was found in the rate of PSA increase between the two groups, the mean PSA doubling time for the intervention group was substantially longer at the 3-month follow-up visit than that of the controls. **Conclusions:** Men with a increasing PSA level after primary treatment were able to make a change to a prostate-healthy diet, accompanied by increases in QOL. No significant difference was found in the log PSA slope between the two groups; however, the PSA doubling time increased substantially in the intervention group compared with that in the controls. Future trials should examine the effect of the prostate-healthy diet with a larger sample of men for a longer period. copyright 2008 Elsevier Inc. All rights reserved.

Pischon, T, H. Boeing, S. Weikert, et al. **Body Size and Risk of Prostate Cancer in the European Prospective Investigation into Cancer and Nutrition.** *Cancer Epidemiology Biomarkers and Prevention.* 2008 November; 1711: 3252-3261.

Background: Body size has been hypothesized to influence the risk of prostate cancer; however, most epidemiologic studies have relied on body mass index (BMI) to assess adiposity, whereas only a few studies have examined whether body fat distribution predicts prostate cancer. **Methods:** We examined the association of height, BMI, waist and hip circumference, and waist-hip ratio with prostate cancer risk among 129,502 men without cancer at baseline from 8 countries of the European Prospective Investigation into Cancer and Nutrition (EPIC), using Cox regression, with age as time metric, stratifying by study center and age at recruitment, and

adjusting for education, smoking status, alcohol consumption, and physical activity. **Results:** During a mean follow-up of 8.5 years, 2,446 men developed prostate cancer. Waist circumference and waist-hip ratio were positively associated with risk of advanced disease. The relative risk of advanced prostate cancer was 1.06 (95% confidence interval, 1.01-1.1) per 5-cm-higher waist circumference and 1.21 (95% confidence interval, 1.04-1.39) per 0.1-unit-higher waist-hip ratio. When stratified by BMI, waist circumference and waist-hip ratio were positively related to risk of total, advanced, and high-grade prostate cancer among men with lower but not among those with higher BMI (Pinteraction for waist with BMI, 0.25, 0.02, and 0.05, respectively; Pinteraction for waist-hip ratio with BMI, 0.27, 0.22, and 0.14; respectively). **Conclusions:** These data suggest that abdominal adiposity may be associated with an increased risk of advanced prostate cancer. This association may be stronger among individuals with lower BMI; however, this finding needs confirmation in future studies. Copyright copyright 2008 American Association for Cancer Research.

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Colorectal

Cotterchio, M, B. A. Boucher, M. Manno, S. Gallinger, A. B. Okey and P. A. Harper. **Red Meat Intake, Doneness, Polymorphisms in Genes that Encode Carcinogen-Metabolizing Enzymes, and Colorectal Cancer Risk.** *Cancer Epidemiology Biomarkers and Prevention.* 2008 November; 1711: 3098-3107.

Colorectal cancer literature regarding the interaction between polymorphisms in carcinogen-metabolizing enzymes and red meat intake/doneness is inconsistent. A case-control study was conducted to evaluate the interaction between red meat consumption, doneness, and polymorphisms in carcinogen-metabolizing enzymes. Colorectal cancer cases diagnosed 1997 to 2000, ages 20 to 74 years, were identified through the population-based Ontario Cancer Registry and recruited by the Ontario Family Colorectal Cancer Registry. Controls were sex-matched and age group-matched random sample of Ontario population. Epidemiologic and food questionnaires were completed by 1,095 cases and 1,890 controls; blood was provided by 842 and 1,251, respectively. Multivariate logistic regression was used to obtain adjusted odds ratio (OR) estimates. Increased red meat intake was associated with increased colorectal cancer risk [OR (>5 versus [less-than or equal to]2 servings/wk), 1.67 (1.36-2.05)]. Colorectal cancer risk also increased significantly with well-done meat intake [OR (>2 servings/ wk well-done versus [less-than or equal to]2 servings/wk rare-regular), 1.57 (1.27-1.93)]. We evaluated interactions between genetic variants in 15 enzymes involved in the metabolism of carcinogens in overcooked meat (cytochrome P450, glutathione S-transferase, UDP-glucuronosyltransferases, SULT, NAT, mEH, and AHR). CYP2C9 and NAT2 variants were associated with colorectal cancer risk. Red meat intake was associated with increased colorectal cancer risk regardless of genotypes; however, CYP1B1 combined variant and SULT1A1-638G>A variant significantly modified the association between red meat doneness intake and colorectal cancer risk. In conclusion, well-done red meat intake was associated with an increased risk of colorectal cancer regardless of carcinogen- metabolizing genotype, although our data suggest that persons with CYP1B1 and SULT1A1 variants had the highest colorectal cancer risk. Copyright copyright 2008 American Association for Cancer Research.

Shimizu, M, Y. Fukutomi, M. Ninomiya, et al. **Green Tea Extracts for the Prevention of Metachronous Colorectal Adenomas: A Pilot Study.** *Cancer Epidemiology Biomarkers and Prevention.* 2008 November; 1711: 3020-3025.

Background: Experimental studies indicate the chemopreventive properties of green tea extract (GTE) on colorectal cancer. Epidemiologically, green tea consumption of >10 cups daily reduced colorectal cancer risk in Japanese. Because colorectal adenomas are the precursors to most sporadic colorectal cancers, we conducted a randomized trial to determine the preventive effect of GTE supplements on metachronous colorectal adenomas by raising green tea consumption in the target population from an average of 6 cups (1.5 g GTE) daily to [greater-than or equal to]10 cups equivalent (2.5 g GTE) by supplemental GTE tablets. Methods: We recruited 136 patients, removed their colorectal adenomas by endoscopic polypectomy, and 1 year later confirmed the clean colon (i.e., no polyp) at the second colonoscopy. The patients were then randomized into two groups while maintaining their lifestyle on green tea drinking: 71 patients supplemented with 1.5 g GTE per day for 12 months and 65 control patients without supplementation. Follow-up colonoscopy was conducted 12 months later in 125 patients (65 in the control group and 60 in the GTE group). Results: The incidence of metachronous adenomas at the end-point colonoscopy was 31% (20 of 65) in the control group and 15% (9 of 60) in the GTE group (relative risk, 0.49; 95% confidence interval, 0.24-0.99; $P < 0.05$). The size of relapsed adenomas was also smaller in the GTE group than in the control group ($P < 0.001$). No serious adverse events occurred in the GTE group. Conclusion: GTE is an effective supplement for the chemoprevention of metachronous colorectal adenomas. Copyright copyright 2008 American Association for Cancer Research.

Oral / Throat / Esophageal

Garavello, W, E. Lucenteforte, C. Bosetti, et al. **Diet Diversity and the Risk of Laryngeal Cancer: A Case-Control Study from Italy and Switzerland.** *Oral Oncol.* 2009 January; 451: 85-89. Diet diversity (defined as the number of different foods consumed) has been considered an indicator of a healthy diet, and favorably related to the risk of several digestive tract cancers. We analyzed the relation between diet diversity and the risk of laryngeal cancer using data from a case-control study carried out between 1992 and 2000 in Italy and Switzerland. The subjects of the study were 527 patients with histologically confirmed incident cancers of the larynx and 1297 patients admitted for acute, non-neoplastic diseases, unrelated to tobacco or alcohol consumption. Total diversity was computed as the number of different foods (overall and within four food groups, i.e., vegetables, fruit, meat, and cereals) consumed at least once per week. A significant inverse association was observed for vegetable diversity (OR = 0.41, 95% CI: 0.28-0.59, for the highest versus the lowest quartile) and fruit diversity (OR = 0.40, 95% CI: 0.27-0.59). Conversely, a direct association was found for meat diversity (OR = 1.67, 95% CI: 1.11-2.50), while no meaningful association was found for total diet and cereal diversity. The results were consistent across strata of age, alcohol drinking and tobacco smoking. This study suggests that a diet not only rich but also varied in fruit and vegetables is related to a decreased risk of laryngeal cancer risk. copyright 2008 Elsevier Ltd. All rights reserved.

Naganuma, T, S. Kuriyama, M. Kakizaki, et al. **Coffee Consumption and the Risk of Oral, Pharyngeal, and Esophageal Cancers in Japan: The Miyagi Cohort Study.** *Am J Epidemiol.* 2008 Dec 15; 16812: 1425-1432. An inverse association between coffee consumption and the risk of oral, pharyngeal, and esophageal cancers has been suggested in case-control studies, but few results from prospective studies are available. Data from the Miyagi Cohort Study in Japan were used to clarify the association between coffee consumption and the risk of these cancers. Information about coffee consumption was obtained from self-administered food frequency questionnaires in 1990. Among 38,679 subjects aged 40-64 years with no previous history of cancer, 157 cases of oral, pharyngeal, and esophageal cancers were identified during 13.6 years of follow-up. Hazard ratios were estimated by the Cox proportional hazards regression

model. The risk of oral, pharyngeal, and esophageal cancers was inversely associated with coffee consumption. The multivariate-adjusted hazard ratio of these cancers for ≥ 1 cups of coffee per day compared with no consumption was 0.51 (95% confidence interval: 0.33, 0.77). This inverse association was consistent regardless of sex and cancer site and was observed both for subjects who did not drink or smoke and for those who currently drank or smoked at baseline. In conclusion, coffee consumption was associated with a lower risk of oral, pharyngeal, and esophageal cancers, even in the group at high risk of these cancers.

Massage

Stringer, J, R. Swindell and M. Dennis. **Massage in Patients Undergoing Intensive Chemotherapy Reduces Serum Cortisol and Prolactin.** *Psychooncology.* 2008 1710: 1024-1031. Objective: The objective is to identify whether single 20 min massage sessions were safe and effective in reducing stress levels of isolated haematological oncology patients. Design: Based on a randomised controlled trial, 39 patients were randomised to aromatherapy, massage or rest (control) arm. Measures: The measures were serum cortisol and prolactin levels, quality of life (EORTC QLQ - C30) and semi-structured interviews. Primary outcome measure was the fall in serum cortisol levels. Results: A significant difference was seen between arms in cortisol ($P = 0.002$) and prolactin ($p=0.031$) levels from baseline to 30 min post-session. Aromatherapy and massage arms showed a significantly greater drop in cortisol than the rest arm. Only the massage arm had a significantly greater reduction in prolactin than the rest arm. The EORTC QLQ-C30 showed a significant reduction in 'need for rest' for patients in both experimental arms compared with the control arm, whereas the semi-structured interviews identified a universal feeling of relaxation in patients in the experimental arms. Conclusion: This pilot study demonstrated that in isolated haematological oncology patients, a significant reduction in cortisol could be safely achieved through massage, with associated improvement in psychological well-being. The implications are discussed. Copyright copyright 2008 John Wiley & Sons, Ltd.

Nutrition

de Lorgeril, M and P. Salen. **The Mediterranean Diet: Rationale and Evidence for its Benefit** *Curr Atheroscler Rep.* 2008 Dec; 106: 518-522. There is now a consensus about recommending the Mediterranean diet pattern for the prevention of coronary heart disease (CHD) and cancer. The most important aspect of this treatment decision, in contrast with the pharmacologic prevention of CHD (including cholesterol lowering), is that the Mediterranean diet has a striking effect on survival. The main explanation for this is that the Mediterranean diet is protective not only against CHD and cancers but also against other various chronic diseases. Furthermore, the Mediterranean diet appears to be effective at reducing atherosclerosis and the risk of fatal complications (ie, sudden cardiac death and heart failure) of atherosclerosis. Finally, unlike drug therapies, no harmful side effect has been reported following the adoption of this dietary pattern. Many micro- and macronutrients characteristic of the Mediterranean diet interact in a synergistic way to induce states of resistance to chronic diseases. More research is required to understand these complex interplays. [References: 46]

Vitamin D

Kilkinen, A, P. Knekt, M. Heliovaara, et al. **Vitamin D Status and the Risk of Lung Cancer: A Cohort Study in Finland.** *Cancer Epidemiology Biomarkers and Prevention.* 2008 November; 1711: 3274-3278. Experimental data support the suppressing effect of vitamin D on lung carcinogenesis, but epidemiologic evidence is limited. The aim of the present study was to evaluate whether serum 25-hydroxy

vitamin D [25(OH)D] level is associated with the risk of lung cancer in a prospective cohort study in Finland. 25(OH)D levels were measured by RIA from serum collected at baseline (1978-1980) from 6,937 men and women. During a maximum follow-up of 24 years, 122 lung cancers were identified. After adjustment for potential confounders, no overall significant association between vitamin D and lung cancer risk was observed [relative risk (RR) for the highest versus lowest tertile, 0.72; 95% confidence interval (95% CI), 0.43-1.19; P_{trend} = 0.22]. There was a statistically significant interaction between vitamin D and sex (P = 0.02) and age (P = 0.02): serum 25(OH)D level was inversely associated with lung cancer incidence for women (RR, 0.16; 95% CI, 0.04-0.59; P_{trend} < 0.001) and younger participants (RR, 0.34; 95% CI, 0.13-0.90; P_{trend} = 0.04) but not for men (RR, 1.03; 95% CI, 0.59-1.82; P_{trend} = 0.81) or older individuals (RR, 0.92; 95% CI, 0.50-1.70; P_{trend} = 0.79). In conclusion, although there was no overall association between vitamin D and lung cancer risk, women and young participants with a higher level of vitamin D were observed to have a lower lung cancer risk. Although experimental data support the suppressing effect of vitamin D on the development of lung cancer, large epidemiologic studies from different populations with repeated measurements of vitamin D are warranted to confirm this finding. Copyright copyright 2008 American Association for Cancer Research.

Abbas, S, J. Chang-Claude and J. Linseisen. **Plasma 25-Hydroxyvitamin D and Premenopausal Breast Cancer Risk in a German Case-Control Study.** *International Journal of Cancer.* 2009 Jan 1; 1241: 250-255. Laboratory and epidemiological data have linked vitamin D to breast cancer prevention. Beside dietary intake, endogenous production of vitamin D substantially contributes to a subject's vitamin D status. Most studies, however, have assessed dietary intake only. Although differential effects of vitamin D on premenopausal and postmenopausal breast cancer have been discussed, this is the first study to investigate the association of plasma 25-hydroxyvitamin D [25(OH)D], as indicator of the overall vitamin D status, with breast cancer risk with restriction to premenopausal women only. We used data of a population-based case-control study comprising 289 cases and 595 matched controls. Information on sociodemographic and breast cancer risk factors was collected by questionnaire and plasma 25(OH)D was measured by enzyme immunoassay. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using conditional logistic regression. We observed a significant inverse association between breast cancer risk and plasma 25(OH)D concentrations. Compared with the lowest category (or=60 nmol/L) were 0.68 (0.43-1.07), 0.59 (0.37-0.94) and 0.45 (0.29-0.70), respectively (p_{trend}) = 0.0006). The association was shown to be nonlinear (p_(nonlinearity)) = 0.06) in fractional polynomial analysis with a stronger effect in women at low plasma 25(OH)D levels, providing some evidence of a threshold effect (at circa 50 nmol/L). The association was stronger in progesterone receptor negative tumors, with suggestive evidence of effect heterogeneity (p_(heterogeneity)) = 0.05, case-only model). Our findings support a protective effect of vitamin D for premenopausal breast cancer.

Lipworth, L, T. J. Bender, M. Rossi, et al. **Dietary Vitamin D Intake and Cancers of the Colon and Rectum: A Case-Control Study in Italy.** *Nutr Cancer.* 2009 January; 611: 70-75. Epidemiologic evidence indicates that vitamin D is inversely associated with risk of colon or rectal cancer or both. Using data from a case-control study conducted in Italy between 1992 and 1996, we examined the relation between dietary intake of vitamin D and colon and rectal cancer risk. The study population comprised patients with incident colon cancer (n = 1,225) or rectal cancer (n = 728) and 4,154 hospital controls. Odds ratios (OR) and 95% confidence intervals (CI) according to deciles of vitamin D intake were estimated by multiple logistic regression. In addition, we adjusted for intensity of sunlight exposure through stratification by

geographic region of residence, and we computed ORs separately by anatomic subsite within the colon. Adjusted ORs for colon cancer were seen to decrease after the 5th decile of vitamin D intake and reached 0.69 (95% CI = 0.50-0.96) for the 9th and 10th deciles, reflecting a statistically significant inverse trend. The inverse association appeared to be somewhat more pronounced for the proximal than the distal colon and was similar among strata of geographic region and calcium intake. Rectal cancer was unrelated to vitamin D intake in this population. In conclusion, we observed an inverse association between dietary vitamin D intake and colon cancer risk among those with the highest intake levels, which was somewhat unexpected given that these levels were still substantially below the levels considered optimal for colon cancer prevention. Copyright copyright 2009, Taylor & Francis Group, LLC.

CAM of the Month

Biegler, KA, M. A. Chaoul and L. Cohen. **Cancer, Cognitive Impairment, and Meditation** *Acta Oncol.* 2009 481: 18-26. **BACKGROUND AND OBJECTIVES:** Cancer-related cognitive impairment has been acknowledged as a substantial limiting factor in quality of life among cancer patients and survivors. In addition to deficits on behavioral measures, abnormalities in neurologic structure and function have been reported. In this paper, we review findings from the literature on cognitive impairment and cancer, potential interventions, meditation and cognitive function, and meditation and cancer. In addition, we offer our hypotheses on how meditation practice may help to alleviate objective and subjective cognitive function, as well as the advantages of incorporating a meditation program into the treatment of cancer patients and survivors for cancer-related cognitive deficits. **FINDINGS:** Various factors have been hypothesized to play a role in cancer-related cognitive impairment including chemotherapy, reduced hormone levels, proinflammatory immune response, fatigue, and distress. Pharmacotherapies such as methylphenidate or modafinil have been suggested to alleviate cognitive deficits. While initial reports suggest they are effective, some pharmacotherapies have side effects and may not relieve other symptoms associated with multimodal cancer treatment including sleep disturbance, nausea and pain. Several recent studies investigating the effects of meditation programs have reported behavioral and corresponding neurophysiological modulations that may be particularly effective in alleviating cancer-related cognitive impairment. Such programs also have been shown to reduce stress, fatigue, nausea and pain, and improve mood and sleep quality. **CONCLUSIONS:** With the increasing success of cancer treatment and the ability to return to previous family, social, and work activities, symptom management and quality of life are an essential part of survivorship. We propose that meditation may help to improve cancer-related cognitive dysfunction, alleviate other cancer-related sequelae, and should be fully investigated as an adjuvant to cancer treatment. [References: 85]

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