



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.

Thank you to **The Canadian Breast Cancer Foundation BC/Yukon Chapter** for their generous support.



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Breast

Hong, SA, K. Kim, S. J. Nam, G. Kong and M. K. Kim. **A Case-Control Study on the Dietary Intake of Mushrooms and Breast Cancer Risk among Korean Women.** *International Journal of Cancer*. 2008 Feb 15; 1224: 919-923.

To evaluate the association between dietary mushroom intake and breast cancer risk, a total of 362 women between the ages of 30 and 65 years who were histologically confirmed to have breast cancer were matched to controls by age (+/-2 years) and menopausal status. Mushroom intake was measured via a food frequency questionnaire that was administered by well-trained interviewers. The associations between the daily intake and the average consumption frequency of mushrooms with breast cancer risk were evaluated using matched data analysis. Both the daily intake (5th vs. 1st quintile, OR = 0.48, 95% CI = 0.30-0.78, p for trend 0.030) and the average consumption frequency of mushrooms (4th vs. 1st quartile, OR = 0.54, 95% CI = 0.35-0.82, p for trend 0.008) were inversely associated with breast cancer risk after adjustment for education, family history of breast cancer, regular exercise [≥ 22.5 MET (metabolic equivalent)-hr/week], BMI (body mass index, Kg/m²), number of children and whether they are currently smoking, drinking or using multivitamin supplements. Further adjustments were made for energy-adjusted carbohydrate, soy protein, folate and vitamin E levels, which tended to attenuate these results. After a stratification was performed according to menopausal status, a strong inverse association was found in postmenopausal women (OR = 0.16, 95% CI = 0.04-0.54, p for trend = 0.0058 for daily intake; OR = 0.17, 95% CI = 0.05-0.54, p for trend = 0.0037 for average frequency), but not in premenopausal women. In conclusion, the consumption of dietary mushrooms may decrease breast cancer risk in postmenopausal women.

Suzuki, R, T. Rylander-Rudqvist, W. Ye, S. Saji, H. Adlercreutz and A. Wolk. **Dietary Fiber Intake and Risk of Postmenopausal Breast Cancer Defined by Estrogen and Progesterone Receptor Status--a Prospective Cohort Study among Swedish Women.** *International Journal of Cancer*. 2008 Jan 15; 1222: 403-412. There is few data on the association between dietary fiber intake and estrogen receptor

(ER)/progesterone receptor (PR)-defined breast cancer risk. We evaluated the association between dietary fiber and ER/PR-defined breast cancer risk stratified by postmenopausal hormone use, alcohol intake, and family history of breast cancer in the population-based Swedish Mammography Screening Cohort comprising 51,823 postmenopausal women. Fiber intake was measured by food-frequency questionnaire collected in 1987 and 1997. Relative risks (RRs) were estimated by hazard ratio derived from Cox proportional hazard regression models. During an average of 8.3-year follow-up, 1,188 breast cancer cases with known ER/PR status were diagnosed. When comparing the highest to the lowest quintile, we observed non-significant inverse associations between total fiber intake and the risk of all tumor subtypes; the multivariate-adjusted RRs were 0.85 (95% CI: 0.69-1.05) for overall, 0.85 (0.64-1.13) for ER+PR+, 0.83 (0.52-1.31) for ER+PR- and 0.94 (0.49-1.80) for ER-PR-. For specific fiber, we observed statistically significant risk reductions for overall (34%) and for ER+PR+ (38%) for the highest versus lowest quintile of fruit fiber, and non-significant inverse associations for other subtypes of cancer and types of fiber. Among ever-users of postmenopausal hormone (PMH), total fiber intake and especially cereal fiber were statistically significantly associated with approximately 50% reduced risk for overall and ER+PR+ tumors when comparing the highest to the lowest quartile, but no association was observed among PMH never users. Our results suggest that dietary fiber intake from fruit and cereal may play a role in reducing breast cancer risk.

Prostate

Chen, RC, J. A. Clark, J. Manola and J. A. Talcott. **Treatment 'Mismatch' in Early Prostate Cancer: Do Treatment Choices Take Patient Quality of Life into Account?** *Cancer*. 2008 01 Jan; 1121: 61-68. BACKGROUND. Pretreatment urinary, bowel, and sexual dysfunction may increase the toxicity of prostate cancer treatments or preclude potential benefits. Using patient-reported baseline dysfunction from a prospective cohort study, we determined the proportion of patients receiving relatively contraindicated ('mismatched') treatments. METHODS. Baseline obstructive uropathy and bowel dysfunction relatively contraindicate

brachytherapy (BT) and external beam radiation therapy (EBRT), respectively, because they increase patients' vulnerability to treatment-related toxicity. Baseline sexual dysfunction renders moot the intended benefit of nerve-sparing radical prostatectomy (NSRP), which is to preserve sexual function. We categorized patients' clinical circumstances by increasing complexity and counted the mismatches in each, expecting weaker or multiple contraindications to increase mismatched treatments. RESULTS. Of 438 eligible patients, 389 (89%) reported preexisting dysfunction, and more than one-third received mismatched treatments. Mismatches did not significantly increase with clinical complexity, and watchful waiting was very infrequent, even when all treatment options were contraindicated. Patient age and comorbidity, but not preexisting dysfunction, were associated with treatment choice. As expected, mismatched BT and EBRT led to worsened urinary and bowel symptoms, respectively, and NSRP did not improve outcomes after baseline sexual dysfunction. CONCLUSIONS. Pretreatment dysfunction does not appear to reliably influence treatment choices, and patients receiving mismatched treatments had worse outcomes. Further study is needed to determine why mismatched treatments were chosen, including the role of incomplete patient-physician communication of baseline dysfunction, and whether using a validated questionnaire before treatment decision-making would bypass this difficulty. Treatment mismatch may be a useful outcome indicator of the quality of patient-centered decisions.

Galvao, DA, D. R. Taaffe, N. Spry and R. U. Newton. **Exercise can Prevent and Even Reverse Adverse Effects of Androgen Suppression Treatment in Men with Prostate Cancer.** *Prostate Cancer and Prostatic Diseases*. 2007 Dec; 104: 340-346. Side effects accompanying androgen deprivation therapy (ADT), including sarcopenia, loss of bone mass and reduction in muscle strength, can compromise physical function, particularly in older patients. Exercise, specifically resistance training, may be an effective and cost-efficient strategy to limit or even reverse some of these adverse effects during and following therapy. In this review, we discuss common morphological and physiological ADT-related side effects or 'Androgen Deprivation and Sarcopenia-Related Disorders' and the existing clinical trials incorporating physical exercise in prostate cancer patients receiving active therapy. Further, training concepts and guidelines are provided for prescribing resistance exercise programs for this population.

Northouse, LL, D. W. Mood, A. Schafenacker, et al. **Randomized Clinical Trial of a Family Intervention for Prostate Cancer Patients and their Spouses.** *Cancer*. 2007 15 Dec; 11012: 2809-2818.

BACKGROUND. Few intervention studies have been conducted to help couples manage the effects of prostate cancer and maintain their quality of life. The objective of this study was to determine whether a family-based intervention could improve appraisal variables (appraisal of illness or caregiving, uncertainty, hopelessness), coping resources (coping strategies, self-efficacy, communication), symptom distress, and quality of life in men with prostate cancer and their spouses. METHODS. For this clinical trial, 263 patient-spouse dyads were stratified by research site, phase of illness, and treatment; then, they were randomized to the control group (standard care) or the experimental group (standard care plus a 5-session family intervention). The intervention targeted couples' communication, hope, coping, uncertainty, and symptom management. The final sample consisted of 235 couples: 123 couples in the control group and 112 couples in the experimental group. Data collection occurred at baseline before randomization and at 4 months, 8 months, and 12 months. RESULTS. At 4-month follow-up, intervention patients reported less uncertainty and better communication with spouses than control patients, but they reported no other effects. Intervention spouses reported higher quality of life, more self-efficacy, better communication, and less negative appraisal of caregiving, uncertainty, hopelessness, and

symptom distress at 4 months compared with controls, and some effects were sustained to 8 months and 12 months. CONCLUSIONS. Men with prostate cancer and their spouses reported positive outcomes from a family intervention that offered them information and support. Programs of care need to be extended to spouses who likely will experience multiple benefits from intervention.

Peters, U, A. J. Littman, A. R. Kristal, R. E. Patterson, J. D. Potter and E. White. **Vitamin E and Selenium Supplementation and Risk of Prostate Cancer in the Vitamins and Lifestyle (VITAL) Study Cohort.** *Cancer Causes and Control*. 2008 Feb; 191: 75-87. Objective: Vitamin E and selenium are promising nutrients for the prevention of prostate cancer, and both are currently being tested in a large randomized trial for prostate cancer. However, results are not expected for at least 6 years. We aimed to investigate the association of vitamin E and selenium supplementation with prostate cancer in the VITamins And Lifestyle (VITAL) study, a cohort study specifically designed to examine supplement use and future cancer risk. Methods: In a prospective design, 35,242 men recruited between 2000 and 2002 from western Washington State completed a questionnaire, including detailed questions about vitamin E and selenium supplement intake during the past 10 years from brand-specific multivitamins and single supplements. Using linkage to the western Washington SEER cancer registry, we documented 830 new cases of prostate cancer from baseline through December 2004. Results: A 10-year average intake of supplemental vitamin E was not associated with a reduced prostate cancer risk overall [hazard ratio (HR) 0.86, 95% confidence interval (CI) 0.65-1.1 for [greater-than or equal to]400 IU/day vs. non-use, p for trend 0.36]; however, risk for advanced prostate cancer (regionally invasive or distant metastatic, n = 123) decreased significantly with greater intake of supplemental vitamin E (HR 0.43, 95% CI 0.19-1.0 for 10-year average intake [greater-than or equal to]400 IU/day vs. non-use, p for trend 0.03). There was no association between selenium supplementation and prostate cancer risk (HR 0.90, 95% CI 0.62-1.3 for 10-year average intake >50 mug/day vs. non-use, p for trend 0.97). Conclusions: In this prospective cohort, long-term supplemental intake of vitamin E and selenium were not associated with prostate cancer risk overall; however, risk of clinically relevant advanced disease was reduced with greater long-term vitamin E supplementation.

 Thank you to the **BC Foundation for Prostate Disease** for their generous support.
www.BCPROSTATECANCER.org

Ovarian

Reb, AM **Transforming the Death Sentence: Elements of Hope in Women with Advanced Ovarian Cancer** *Oncol Nurs Forum*. 2007 11; 346: E70-81.

PURPOSE/OBJECTIVES: To describe the experience of hope in women with advanced ovarian cancer. RESEARCH APPROACH: Grounded theory methodology with interviews. SETTING: Oncology clinics in the northeastern United States. PARTICIPANTS: 20 women aged 42-73 who had completed initial chemotherapy and had no evidence of recurrence. METHODOLOGIC APPROACH: A personal data form and focused interview guide supported data collection. The core variable and related themes were identified using the constant comparative process. Demographic and treatment information was analyzed using descriptive statistics. MAIN RESEARCH VARIABLES: The process of hope in women with advanced ovarian cancer. FINDINGS: Facing the death sentence emerged as the main concern. The core variable in dealing with the concern was transforming the death threat. The three phases of the trajectory were shock (reverberating from the impact), aftershock (grasping reality), and rebuilding (living the new paradigm). Healthcare provider communication and spirituality influenced women's

abilities to transform the death sentence. Support and perceived control emerged as key dimensions of the core variable. Conclusions: Women experience significant distress and trauma symptoms associated with a diagnosis of ovarian cancer. Hope was linked closely to the core variable and was necessary for finding meaning in the experience. Women with high support and perceived control seemed most hopeful and able to transform the death sentence. INTERPRETATIONS: Evidence-based interventions and strategies are needed to foster improved provider communication, symptom management, and peer support for women facing ovarian cancer. Future nursing research should focus on strategies that enhance support, perceived control, hope, and spirituality.

Gastric

Kim, HJ, S. S. Lee, B. Y. Choi and M. K. Kim. **Nitrate Intake Relative to Antioxidant Vitamin Intake Affects Gastric Cancer Risk: A Case-Control Study in Korea.** *Nutr Cancer.* 2007 592: 185-191.

The objective of this study was to determine whether the intake of nitrate relative to antioxidant vitamin rather than absolute intake of nitrate affects the risk of gastric cancer (GC). In a case-control study in Korea using a food frequency questionnaire, trained dietitians interviewed 136 GC cases and an equal number of controls matched by sex and age. As an index of nitrate intake relative to antioxidant vitamins intake, we calculated the nitrate:antioxidant vitamin consumption ratio. The mean daily nitrate intake from foods was very high in our subjects. Higher absolute intake of nitrate was not associated with GC risk [odds ratios (OR) = 1.13; 95% confidence interval (CI) = 0.42-3.06]. However, the GC risk distinctly increased as the nitrate:antioxidant vitamin consumption ratio increased, particularly with higher nitrate: vitamin E (OR = 2.78; 95% CI = 1.01-7.67) and nitrate:folate ratios (OR = 3.37; 95% CI = 1.28-8.87). Therefore, GC risk was influenced by the intake of nitrate relative to antioxidant vitamins. Our results suggest that a decrease in the intake of nitrate relative to antioxidant vitamins is considerably more effective in reducing GC risk than either a lower absolute intake of nitrate or a higher intake of antioxidant vitamins alone.

Endometrial

Lucenteforte, E, R. Talamini, M. Montella, et al. **Macronutrients, Fatty Acids and Cholesterol Intake and Endometrial Cancer.** *Annals of Oncology.* 2008 Jan; 191: 168-172. Background: There is some evidence that dietary habits may influence the risk of endometrial cancer independently of body mass, although the role of diet on endometrial carcinogenesis is unclear. Patients and methods: We carried out a multicenter case-control study from 1992 to 2006 in Italy on 454 women with incident, histologically confirmed endometrial cancer (age range 18-79 years) and 908 controls (age range 19-79 years) admitted to hospitals for acute, non-neoplastic diseases. A validated food-frequency questionnaire was used to estimate macronutrients, fatty acids and cholesterol intake. Logistic regression models, conditioned on age and study centre, and adjusted for major known risk factor of endometrial cancer and residual of energy intake were used to estimate odds ratios (OR) and 95% confidence intervals (CI). Results: Significant direct associations were observed with intake of energy (OR = 1.7 for the highest versus the lowest quintile, 95% CI = 1.1-2.5), and cholesterol (OR = 2.1, 95% CI = 1.4-3.2), while a direct borderline association emerged with saturated fatty acids (OR = 1.3, 95% CI = 0.9-2.0). There was no association with proteins, sugars, starch, total fat and other selected fatty acids. Conclusion: Energy and cholesterol intake were associated with endometrial cancer.

Psychosocial

Carlson, LE, M. Speca, P. Faris and K. D. Patel. **One Year Pre-Post Intervention Follow-Up of Psychological, Immune, Endocrine and Blood Pressure Outcomes of Mindfulness-Based Stress Reduction (MBSR) in Breast and Prostate Cancer Outpatients.** *Brain, Behavior, & Immunity.* 2007 Nov; 218: 1038-1049.

OBJECTIVES: This study investigated the ongoing effects of participation in a mindfulness-based stress reduction (MBSR) program on quality of life (QL), symptoms of stress, mood and endocrine, immune and autonomic parameters in early stage breast and prostate cancer patients. METHODS: Forty-nine patients with breast cancer and 10 with prostate cancer enrolled in an eight-week MBSR program that incorporated relaxation, meditation, gentle yoga and daily home practice. Demographic and health behaviors, QL, mood, stress symptoms, salivary cortisol levels, immune cell counts, intracellular cytokine production, blood pressure (BP) and heart rate (HR) were assessed pre- and post-intervention, and at 6- and 12-month follow-up. RESULTS: Fifty-nine, 51, 47 and 41 patients were assessed pre- and post-intervention and at 6- and 12-month follow-up, respectively, although not all participants provided data on all outcomes at each time point. Linear mixed modeling showed significant improvements in overall symptoms of stress which were maintained over the follow-up period. Cortisol levels decreased systematically over the course of the follow-up. Immune patterns over the year supported a continued reduction in Th1 (pro-inflammatory) cytokines. Systolic blood pressure (SBP) decreased from pre- to post-intervention and HR was positively associated with self-reported symptoms of stress. CONCLUSIONS: MBSR program participation was associated with enhanced quality of life and decreased stress symptoms, altered cortisol and immune patterns consistent with less stress and mood disturbance, and decreased blood pressure. These pilot data represent a preliminary investigation of the longer-term relationships between MBSR program participation and a range of potentially important biomarkers.

Epstein, DR and S. R. Dirksen. **Randomized Trial of a Cognitive-Behavioral Intervention for Insomnia in Breast Cancer Survivors** *Oncol Nurs Forum.* 2007 09//Sep2007 Online Exclusive; 345: E51-9.

Behavioral intervention for treating insomnia in breast cancer survivors. Design: Randomized controlled trial. Setting: University and medical center settings. Sample: 72 women at least three months after primary treatment for breast cancer with sleep-onset or sleep maintenance insomnia at least three nights per week for at least three months as determined through daily sleep diaries. Methods: Random assignment to a multicomponent intervention (stimulus control instructions, sleep restriction, and sleep education and hygiene) or a single-component control group (sleep education and hygiene). Main Research Variables: Sleep-onset latency, wake after sleep onset, total sleep time, time in bed, sleep efficiency, and sleep quality. Findings: After the intervention, both groups improved on sleep-onset latency, wake after sleep onset, total sleep time, time in bed, sleep efficiency, and sleep quality based on daily sleep diaries. A between-group difference existed for time in bed. Wrist actigraph data showed significant pre- to postintervention changes for sleep-onset latency, wake after sleep onset, total sleep time, and time in bed. When compared to the control group, the multicomponent intervention group rated overall sleep as more improved. Conclusions: A nonpharmacologic intervention is effective in the treatment of insomnia in breast cancer survivors. Implications for Nursing: Breast cancer survivors can benefit from a cognitive-behavioral intervention for chronic insomnia. Sleep education and hygiene, a less complex treatment than a multicomponent intervention, also is effective in treating insomnia.

Nutrition

Lila, MA **From Beans to Berries and Beyond: Teamwork between Plant Chemicals for Protection of Optimal Human Health** *Ann N Y Acad Sci.* 2007 Oct; 1114372-380.

It is now well known to consumers around the world that certain fruits and vegetables can help prevent or treat chronic human diseases. But, what many people don't fully appreciate is that it is not a single component in these plant-derived foods, but rather complex mixtures of interacting natural chemicals, that produce such powerful health-protective effects. These natural components accumulate simultaneously together in a plant, and provide a multifaceted defensive strategy for both the plant, and the human consumer. In order to investigate the strength of natural chemical cooperation in highly-pigmented, flavonoid-rich functional foods, our lab has relied on analysis of both whole fruits, and continuous, reliable plant cell culture production systems which accumulate anthocyanins and proanthocyanidins in high concentrations. Successive rounds of relatively gentle, rapid, and large-volume fractionations are linked to bioassay of complex to simple mixtures and semi-purified compounds. By means of this strategy, additive interactions or synergies between related compounds in health maintenance can be sorted out. Interestingly, phytochemical interactions between the same classes of compounds intensify the efficacy of flavonoid-rich fruits against multiple, not necessarily discrete, human disease conditions including CVD, cancer, metabolic syndrome, and others. [References: 30]

Waterman, E and B. Lockwood. **Active Components and Clinical Applications of Olive Oil.** *Alternative Medicine Review.* 2007 Dec; 124: 331-342.

The olive tree, *Olea europaea*, is native to the Mediterranean basin and parts of Asia Minor. The fruit and compression-extracted oil have a wide range of therapeutic and culinary applications. Olive oil also constitutes a major component of the "Mediterranean diet." The chief active components of olive oil include oleic acid, phenolic constituents, and squalene. The main phenolics include hydroxytyrosol, tyrosol, and oleuropein, which occur in highest levels in virgin olive oil and have demonstrated antioxidant activity. Antioxidants are believed to be responsible for a number of olive oil's biological activities. Oleic acid, a monounsaturated fatty acid, has shown activity in cancer prevention, while squalene has also been identified as having anticancer effects. Olive oil consumption has benefit for colon and breast cancer prevention. The oil has been widely studied for its effects on coronary heart disease (CHD), specifically for its ability to reduce blood pressure and low-density lipoprotein (LDL) cholesterol. Antimicrobial activity of hydroxytyrosol, tyrosol, and oleuropein has been demonstrated against several strains of bacteria implicated in intestinal and respiratory infections. Although the majority of research has been conducted on the oil, consumption of whole olives might also confer health benefits.

Acupuncture

Molassiotis, A, P. Sylt and H. Diggins. **The Management of Cancer-Related Fatigue After Chemotherapy with Acupuncture and Acupressure: A Randomised Controlled Trial.** *Complement Ther Med.* 2007 Dec; 154: 228-237.

Background: Cancer-related fatigue after chemotherapy is a difficult symptom to manage in practice and the most disruptive symptom in patients' lives. Acupuncture is a popular complementary therapy among cancer patients and some evidence exists that it could potentially alleviate fatigue by stimulating 'energy' points in the body. Hence, this study was carried out to assess the effects of acupuncture and acupressure in managing cancer-related fatigue and the feasibility of running a randomised trial with these two complementary therapies in preparation for a large trial. Methods: This study was a randomised controlled trial. Forty-seven patients with cancer who experienced moderate to

severe fatigue were randomised either to an acupuncture group (n = 15), an acupressure group (n = 16) or a sham acupressure group (n = 16). The acupuncture group received six 20-min sessions over 2 weeks, while the patients in the two acupressure groups were taught to massage/press the points and did so daily thereafter for 2 weeks on their own. Patients completed the Multidimensional Fatigue Inventory before randomisation, at the end of the 2-week intervention and again about 2 weeks after the end of the intervention. Results: Significant improvements were found with regards to General fatigue (P < 0.001), Physical fatigue (P = 0.016), Activity (p = 0.004) and Motivation (P = 0.024). At the end of the intervention, there was a 36% improvement in fatigue levels in the acupuncture group, while the acupressure group improved by 19% and the sham acupressure by 0.6%. Improvements were observed even 2 weeks after treatments, although they were lower (22%, 15%, 7%, respectively). Acupuncture was a more effective method than acupressure or sham acupressure. Subjects needed a longer treatment period to have more sustained results. The trial was methodologically feasible. Conclusion: Acupuncture shows great potential in the management of cancer-related fatigue. As a randomised trial with acupuncture is feasible and preliminary data shows significant improvements, it should be tested further using a large sample and a multicentre design.

CAM of the Month

Ayers, TA **A Partnership in Like-Minded Thinking-Generating Hopefulness in Persons with Cancer.** *Medicine, Health Care & Philosophy.* 2007 Mar; 101: 65-80.

A conceptual model of a partnership in 'like-minded thinking' consists of the following components: a relationship, a shared goal with mutual agreement to work toward that goal, and reciprocal encouragement between two people. A like-minded alliance is a relationship that offers support while at the same time encourages hope and establishes a reciprocating emotional attitude of hopefulness. The discussion focuses on the principles of such a model that is designed primarily as a lay intervention for anyone who has a close friend with cancer and who wants to assist the friend in maintaining a hopeful attitude in the face of illness. While this model is not directed at healthcare professionals it may be transferable into psychosocial interventions to assist persons toward sustaining hopefulness in the context of the cancer trajectory. Much has been written in the literature about how hopelessness spawns despair for individuals who have cancer and in those near the end of life; it may even create a desire for hastened death (Breitbart W., Heller K.S.: 2003, 'Reframing Hope: Meaning-Centered Care for Patients Near the End of Life'. *Journal of Palliative Medicine* 6, 979-988; Jones J.M., Huggins M.A., Rydall A.C., Rodin G.M.: 2003, 'Symptomatic distress, hopelessness, and the desire for hastened death in hospitalized cancer patients', *Journal of Psychosomatic Research* 55, 411-418). Therefore, the aim of this paper is to explore how like-minded thinking for a person with cancer and his or her support person provides a framework for a personal shared worldview that is hope-based, meaningful and coherent.

InspireHealth provides an integrated whole person approach to health for individuals living with cancer. Our medical doctors guide patients to explore and learn about a variety of wellness approaches to health and healing in addition to conventional cancer treatment. This integrated medical model, which engages people in their own care, improves quality of life and reduces the likelihood of cancer recurrence. The editorial board includes: Dr. Hal Gunn, CEO and Co-founder, Dr. Janice Wright, Dr. Teresa Clarke and Dr. Ron Puhky.

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