

REsearch UPDATES

FOR THE LATEST IN WORLDWIDE INTEGRATED CANCER CARE

INSide

| | |
|------------------------------------|-----|
| Inspiring News | 1 |
| Prostate Cancer | 2 |
| Breast Cancer | 2,3 |
| Colorectal Cancer | 3 |
| Melanoma | 3 |
| Oral Cancer | 4 |
| Acupuncture | 4,5 |
| Traditional Chinese Medicine | 5 |
| Ayurvedic Treatment | 6 |
| Vitamin D | 6 |
| STUDY OF THE MONTH | 7 |

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

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InspireHealth
INTEGRATED CANCER CARE

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Inspiring Access to Integrative Cancer Care

The British Columbia Government is funding the expansion of InspireHealth with the goal of providing access to integrative care for all BC residents living with cancer—a first in the world.

InspireHealth is honoured and excited to report that thanks to the support of the Ministry of Health and the BC provincial government, we will soon be opening five new integrative cancer care centres throughout BC. The provincial government will provide one-time, start-up funding for the new centres along with additional annual funding to support up to 12 new InspireHealth physicians.



Left to right: Hon. Michael de Jong, Health Minister; Hal Gunn, InspireHealth CEO; Fiona Walks, Vice President Safety, Quality and Supportive Care, BC Cancer Agency; Carol Sicoli, InspireHealth patient; Dr. Margaret MacDiarmid, Vancouver-Fairview MLA.

InspireHealth's new integrative cancer care centres will open in Victoria, Kelowna, Abbotsford, and Prince George, with all of the centres open by September 2012. In addition, we will be establishing a 'virtual' InspireHealth centre to serve rural and remote parts of British Columbia, and will be adding more services and staff to our Vancouver centre.

"Integrative cancer care is part of our commitment to support British Columbians and encourage them to make healthier choices," stated BC Minister of Health Michael de Jong. "Integrative cancer care provides cancer patients with access to improved physical, emotional and nutritional health as well as new opportunities for patients to engage with practitioners about natural therapy interventions and healthy lifestyles."

Over the past 14 years, we at InspireHealth have remained passionately connected to our larger vision—to provide integrative care to all British Columbians living with cancer. We've recognized that health is more than the treatment of illness. An optimal healthcare system includes the broader support of health. Together, we've recognized the essential role that patients themselves can play in their own health and healing. We know that supporting body, mind, spirit and health is as important as standard cancer treatment.

Many times, supporters have asked, "Why isn't InspireHealth available to all cancer patients? Why isn't it a part of standard care?" They say this because they know that our patients do better, live longer, and are inspired by life.

"An integrative approach to cancer care supports the mind, body, spirit and immune system," said Dr. Hal Gunn, co-founder and CEO of InspireHealth. "There is growing evidence that the widespread adoption of InspireHealth's integrative approach to cancer care will result in a significant reduction in cancer deaths, cancer recurrences, and related healthcare costs."

Through your interest and support, we are transforming the conception of optimal cancer care to include the support of mind, body, spirit and health. Through this new funding initiative, BC will become the world leader in integrative care—a model for the rest of the world.

PROSTATE CANCER

Dhillon, PK, S. A. Kenfield, M. J. Stampfer, et al.

Long-Term Aspirin use and the Risk of Total, High-Grade, Regionally Advanced and Lethal Prostate Cancer in a Prospective Cohort of Health Professionals, 1988-2006.

International Journal of Cancer. 2011 01 May 2011; 12810: 2444-2452.

BACKGROUND: Experimental studies suggest a role for aspirin in the chemoprevention of prostate cancer and epidemiological evidence supports a modest inverse association between regular aspirin use and prostate cancer risk, especially for advanced disease. **METHODS:** In a prospective cohort study of 51,529 health professionals aged 40-75 years at baseline, we evaluated long-term aspirin use and the incidence of total, high-grade (Gleason 8-10, n = 488), regionally advanced (T3b-T4 or N1, n = 228) and lethal prostate cancer (M1, bony metastases or prostate cancer death, n = 580) from 1988-2006. We used Cox proportional hazards regression to evaluate risk associated with frequency (days/week), quantity (tablets/week), recency and duration of aspirin use after multivariable adjustment for confounders and other predictors of prostate cancer risk.

RESULTS: A total of 4,858 men were diagnosed with prostate cancer during the 18-year study period. Men taking ≥ 2 adult-strength aspirin tablets a week had a 10% lower risk of prostate cancer (p -for-trend = 0.02). For regionally advanced cancer, we observed no significant associations with aspirin use. For high-grade and lethal disease, men taking ≥ 6 adult-strength tablets/week experienced similar reductions in risk hazard ratio [HR = 0.72 (95% confidence intervals [CI]: 0.54, 0.96) and HR = 0.71 (95% CI: 0.50, 1.00)]. Analytical approaches to address bias from more frequent prostate-specific antigen screening among aspirin users did not yield different conclusions. We observed reductions in the risk of high-grade and lethal prostate cancer associated with higher doses of aspirin, but not with greater frequency or duration, in a large, prospective cohort of health professionals.

CONCLUSION: Our data support earlier observations of modest inverse associations with advanced prostate cancer.

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BREAST CANCER

Kwan, ML, L. H. Kushi, E. Weltzien, et al.

Alcohol Consumption and Breast Cancer Recurrence and Survival among Women with Early-Stage Breast Cancer: The Life After Cancer Epidemiology Study.

Journal of Clinical Oncology. 2010 10 Oct 2010; 2829: 4410-4416.

PURPOSE: To examine the association of alcohol consumption after breast cancer diagnosis with recurrence and mortality among early-stage breast cancer survivors. **PATIENTS AND METHODS:** Patients included 1,897 LACE study participants diagnosed with early-stage breast cancer between 1997 and 2000 and recruited on average 2 years post diagnosis, primarily from the Kaiser Permanente Northern California Cancer Registry. Alcohol consumption (i.e., wine, beer, and liquor) was assessed at cohort entry using a food frequency questionnaire. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% CI with adjustment for known prognostic factors.

RESULTS: Two hundred ninety-three breast cancer recurrences and 273 overall deaths were ascertained after an average follow-up of 7.4 years. Nine hundred fifty-eight women (51%) were considered drinkers (> 0.5 g/d of alcohol), and the majority drank wine (89%). Drinking ≥ 6 g/d of alcohol compared with no drinking was associated with an increased risk of breast cancer recurrence (HR, 1.35; 95% CI, 1.00 to 1.83) and death due to breast cancer (HR, 1.51; 95% CI, 1.00 to 2.29). The increased risk of recurrence appeared to be greater among postmenopausal (HR, 1.51; 95% CI, 1.05 to 2.19) and overweight and obese women (HR, 1.60; 95% CI, 1.08 to 2.38). Alcohol intake was not associated with all-cause death and possibly associated with decreased risk of non-breast cancer death.

CONCLUSION: Consuming three to four alcoholic drinks or more per week after a breast cancer diagnosis may increase risk of breast cancer recurrence, particularly among postmenopausal and overweight/obese women, yet the cardioprotective effects of alcohol on non-breast cancer death were suggested.





Ronco, AL, E. De Stefani, D. Aune, et al.

Nutrient Patterns and Risk of Breast Cancer in Uruguay.

Asian Pacific Journal of Cancer Prevention. 2010 2010; 112: 519-524.

OBJECTIVES: To explore the role of nutrient patterns in the etiology of breast cancer (BC) among Uruguayan women. **METHODS:** A principal component analysis was conducted. The study included 442 newly diagnosed cases of BC and 442 hospitalized controls.

RESULTS: Two dietary patterns derived from factor analysis and were labeled as high-meat and antioxidants patterns. Whereas the high-meat pattern was directly associated with BC risk (OR for the highest versus the lowest quartile = 3.50, 95 % CI 1.94-6.30, p-value for trend <0.0001), the antioxidants pattern displayed a protective effect (OR=0.44, 95 % CI 0.27-0.74). Its negative association was stronger for postmenopausal than for premenopausal women (OR=0.63, 95% CI 0.51-0.79 vs. OR=0.89, 95% CI 0.50-1.56, respectively). Both strata were heterogeneous (p=0.004). The high-meat pattern was more associated with BC risk among patients with family history of BC compared with participants without it, but results did not differ by histology. In contrast, the antioxidants pattern was more associated with non-ductal cancers (OR=0.50 [95 % CI 0.35-0.69]) than with ductal cancers (OR=0.72, 95 % CI 0.58-0.88, heterogeneity p-value=0.03).

CONCLUSIONS: Results support an association between the high-meat and antioxidant dietary patterns and BC risk. Furthermore, findings suggest that gene-environmental interactions may be important in BC etiology.

COLORECTAL CANCER

Lee, JE, W. C. Willett, C. S. Fuchs, et al.

Folate Intake and Risk of Colorectal Cancer and Adenoma: Modification by Time.

Am J Clin Nutr. 2011 01 Apr 2011; 934: 817-825.

BACKGROUND: Experimental and observational studies have suggested that folate may play dual roles in colorectal cancer risk depending on the timing and dose. **OBJECTIVE:** We examined the latency between folate intake and the incidence of colorectal cancer. **DESIGN:** We prospectively examined associations between folate intake assessed every 2 to 4 y by using validated food-frequency questionnaires and risk of colorectal cancer and adenoma in the Nurses' Health Study and Health Professionals Follow-Up Study, which included 2299 incident colorectal cancers and 5655 colorectal adenomas from 1980 to 2004.

RESULTS: There was an association between total folate intake 12-16 y before diagnosis and lower risk of colorectal cancer (relative risk: 0.69; 95% CI: 0.51, 0.94; ≥ 800 compared with < 250 μg folate/d). The current use of multivitamins for > 15 y, but not a shorter duration of use, was associated with lower risk of colorectal cancer; and a shorter duration of use was related to lower risk of adenoma. We did not observe an adverse effect of total folate or synthetic folic acid on risk of colorectal cancer or adenoma even during the folic acid fortification era.

CONCLUSION: Folate intake is inversely associated with risk of colorectal cancer only during early preadenoma stages.

MELANOMA

Cust, AE, B. K. Armstrong, C. Goumas, et al.

Sunbed use during Adolescence and Early Adulthood is Associated with Increased Risk of Early-Onset Melanoma.

International Journal of Cancer. 2011 01 May 2011; 12810: 2425-2435.

Sunbed use is associated with increased risk of melanoma. Younger people might be more susceptible to the carcinogenic effects of ultraviolet radiation. We investigated the association between sunbed use and risk of early-onset cutaneous malignant melanoma. From the Australian Melanoma Family Study, a multicentre, population-based, case-control-family study, we analysed data for 604 cases diagnosed between ages 18 and 39 years and 479 controls.



Data were collected by interview. Associations were estimated as odds ratios (ORs) using unconditional logistic regression, adjusting for age, sex, city, education, family history, skin color, usual skin response to sunlight and sun exposure. Compared with having never used a sunbed, the OR for melanoma associated with ever-use was 1.41 (95% confidence interval (CI) 1.01-1.96), and 2.01 (95% CI 1.22-3.31) for more than 10 lifetime sessions (P_{trend} 0.01 with cumulative use).

The association was stronger for earlier age at first use (P_{trend} 0.02). The association was also stronger for melanoma diagnosed when aged 18-29 years (OR for more than 10 lifetime sessions = 6.57, 95% CI 1.41-30.49) than for melanoma diagnosed when 30-39 years (OR 1.60, 95% CI 0.92-2.77; $P_{\text{interaction}}$ 0.01). Among those who had ever used a sunbed and were diagnosed between 18 and 29 years of age, three quarters (76%) of melanomas were attributable to sunbed use.

Sunbed use is associated with increased risk of early-onset melanoma, with risk increasing with greater use, an earlier age at first use and for earlier onset disease.

ORAL CANCER

Edefonti, V, F. Bravi, C. La Vecchia, et al.

Nutrient-Based Dietary Patterns and the Risk of Oral and Pharyngeal Cancer.

Oral Oncol. 2010 May; 465: 343-348.

BACKGROUND: The relationship between diet and oral and pharyngeal cancer has been rarely addressed considering dietary patterns. **METHODS:** We examined this issue using data from a case-control study carried out between 1992 and 2005. Cases were 804 incident oral cancers hospitalized in 3 Italian areas. Controls were 2080 subjects hospitalized for non-neoplastic diseases. Dietary habits were investigated through a validated 78-item food-frequency questionnaire. Overall and individual measures of sampling adequacy were calculated to assess if applying a factor analysis or not. A posteriori dietary patterns were identified through a principal component factor analysis performed on a selected set of 29 nutrients. The internal reproducibility, robustness and reliability of the identified patterns were evaluated. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using unconditional multiple logistic regression models on quintiles of factor scores. The measures of sampling adequacy were generally satisfactory.

RESULTS: We identified five major dietary patterns named Animal products, Starch-rich, Vitamins and fiber, Unsaturated fats and Retinol and niacin. The Animal products pattern was positively associated with oral cancer (OR=1.56, 95% CI: 1.13-2.15 for the highest vs. the lowest score quintile), whereas the Starch-rich pattern (OR=0.71, 95% CI: 0.50-0.99), the Vitamins and fiber pattern (OR=0.47, 95% CI: 0.34-0.65) and the Unsaturated fats pattern (OR=0.63, 95% CI: 0.45-0.86) were inversely associated with it.

CONCLUSION: These findings confirm that diets rich in animal origin and animal fats are positively, and those rich in fruit and vegetables, and vegetable fats inversely related to oral and pharyngeal cancer risk.

ACUPUNCTURE

Enblom, A, M. Lekander, M. Hammar, et al.

Getting the Grip on Nonspecific Treatment Effects: Emesis in Patients Randomized to Acupuncture Or Sham Compared to Patients Receiving Standard Care.

PLoS ONE. 4766 Article Number: e1; 6 (3) , 2011 Date of Publication: 2011.

BACKGROUND: It is not known whether or not delivering acupuncture triggers mechanisms cited as placebo and if acupuncture or sham reduces radiotherapy-induced emesis more than standard care.

METHODOLOGY/PRINCIPAL FINDINGS: Cancer patients receiving radiotherapy over abdominal/pelvic regions were randomized to verum (penetrating) acupuncture (n = 109; 99 provided data) in the alleged antiemetic acupuncture point PC6 or sham acupuncture (n = 106; 101 provided data) performed with a telescopic non-penetrating needle at a sham point 2-3 times/week during the whole radiotherapy period. The acupuncture cohort was compared to a reference cohort receiving standard care (n = 62; 62 provided data). The occurrence of emesis in each group was compared after a mean dose of 27 Gray. Nausea and vomiting were experienced during the preceding week by 37 and 8% in the verum acupuncture group, 38



and 7% in the sham acupuncture group and 63 and 15% in the standard care group, respectively. The lower occurrence of nausea in the acupuncture cohort (verum and sham) compared to patients receiving standard care (37% versus 63%, relative risk (RR) 0.6, 95% confidence interval (CI) 0.5-0.8) was also true after adjustment for potential confounding factors for nausea (RR 0.8, CI 0.6 to 0.9). Nausea intensity was lower in the acupuncture cohort (78% no nausea, 13% a little, 8% moderate, 1% much) compared to the standard care cohort (52% no nausea, 32% a little, 15% moderate, 2% much) ($p = 0.002$). The acupuncture cohort expected antiemetic effects from their treatment (95%). Patients who expected nausea had increased risk for nausea compared to patients who expected low risk for nausea (RR 1.6; CI 1.2-2.4).

CONCLUSIONS/SIGNIFICANCE: Patients treated with verum or sham acupuncture experienced less nausea and vomiting compared to patients receiving standard care, possibly through a general care effect or due to the high level of patient expectancy. Trial Registration: ClinicalTrials.gov NCT00621660.



Stone, JAM, G. L. Gettelfinger and P. A. S. Johnstone.

Treatment of 13 Patients with Post-Herpetic Neuralgia using Acupuncture.

Journal of the Society for Integrative Oncology. 2010 Fall 2010; 84: 126-130.

OBJECTIVES/BACKGROUND: Postherpetic neuralgia (PHN) is a painful complication of the varicella zoster virus, often occurring in weakened and immunocompromised patients. As cancer patients are at high risk for developing zoster, PHN is a complication faced by patients and their caregivers. While a wide variety of therapeutic approaches have been advocated over the years, most have not been found to be effective.

PATIENTS/METHODS: This retrospective series discusses the successful treatment of 13 patients-including seven cancer patients-with PHN, using acupuncture. Patients were treated by a single practitioner in a conventional community pain practice. Needling was performed along the affected dermatome. Therapy occurred twice-weekly for 1-2 weeks, then less frequently until pain relief was optimized.

RESULTS: Patients received a median of 7 treatments (range 4-11). Median baseline allodynia levels were reduced from 7/10 (range 5 to 9) to zero (range 0 to 6), intermittent shooting pain from 9/10 (range 7 to 10) to 1/10 (range 0 to 6). 7 of 10 patients (70%) were able to be weaned off pain medications.

CONCLUSIONS: These data support acupuncture as an intriguing treatment option for patients suffering from PHN. It is safe for immunocompromised patients and effective in reducing PHN pain with lasting results.

TRADITIONAL CHINESE MEDICINE

Xue, D, H. Sun and P.-P Li.

Long-Term Chinese Herbs Decoction Administration for Management of Hot Flashes Associated with Endocrine Therapy in Breast Cancer Patients.

Chin J Cancer Res. 2011 March 2011; 231: 74-78.

OBJECTIVE: To evaluate the effect of Chinese herbs decoction Shu-Gan-Liang-Xue on endocrine therapy-associated hot flashes symptom in breast cancer patients. **METHODS:** Sixty-six patients with breast cancer receiving adjuvant endocrine therapy were categorized to two groups, the control group received endocrine therapy alone, the other group is administered with Chinese herbs decoction Shu-Gan-Liang-Xue besides the endocrine therapy: Shu-Gan-Liang-Xue decoction was administered above 6 months per year for more than 2 years. Frequency of hot flashes per day was recorded, and the effect of Shu-Gan-Liang-Xue decoction on hot flashes symptom being assessed with Kupperman Scoring Index.

RESULTS: Sixty cases were analyzed, 32 cases in endocrine therapy combining Chinese herbs decoction group, 28 cases in mere endocrine therapy group. For hot flashes symptom, in Chinese herbs decoction administration group, 7 cases (21.9%) reported symptom disappeared, 22 cases (68.7%) reported symptom alleviated, 3 cases (9.4%) reported symptom not changed; in endocrine therapy alone group, 5 cases (17.9%) reported symptom disappeared, 13 cases (46.4%) reported symptom alleviated, 10 cases (10/28, 35.7%) reported symptom not changed. The difference between two groups was statistically significant ($P=0.013$). For sleeping disorder, in Chinese herbs decoction administration group, 27 cases (84.4%) reported symptom improved, 5 cases (15.6%) reported no change; in endocrine therapy alone group, 16



cases (57.1%) symptom improved, 12 cases (42.9%) reported no change in sleeping disorder ($P=0.019$), the difference was also of significance statistically.

CONCLUSION: Long-term Chinese herbs decoction administration remarkably improved hot flashes symptom and sleeping disorder associated with endocrine therapy, meanwhile without definite toxicity and influence on the risk of recurrence of tumor.

AYURVEDIC TREATMENT

Prakash, B, P. M. Parikh and S. K. Pal.

Herbo-Mineral Ayurvedic Treatment in a High Risk Acute Promyelocytic Leukemia Patient with Second Relapse: 12 Years Follow Up.

Journal of Ayurveda and Integrative Medicine. 2010 July-September 2010; 13: 215-218.

A 47 year old diabetic male patient was diagnosed and treated for high risk AML-M3 at Tata Memorial Hospital (BJ 17572), Mumbai in September 1995. His bone marrow aspiration cytology indicated 96% promyelocytes with abnormal forms, absence of lymphocytic series and myeloperoxidase test 100% positive. Initially treated with ATRA, he achieved hematological remission on day 60, but cytogenetically the disease persisted. The patient received induction and consolidated chemotherapy with Daunorubicin and Cytarabine combination from 12.01.96 to 14.05.96, following which he achieved remission.

However, his disease relapsed in February 97. The patient was given two cycles of chemotherapy with Idarubicin and Etoposide, after which he achieved remission. His disease again relapsed in December 97. The patient then refused more chemotherapy and volunteered for a pilot Ayurvedic study conducted by the Central Council for Research in Ayurveda and Siddha, New Delhi. The patient was treated with a proprietary Ayurvedic medicine Navajeevan, Kamadudha Rasa and Keharuba Pisti for one year. For the subsequent 5 years the patient received three months of intermittent Ayurvedic treatment every year.

The patient achieved complete disease remission with the alternative treatment without any adverse side effects. The patient has so far completed 13 years of survival after the start of Ayurvedic therapy.



VITAMIN D

Garland, CF, C. B. French, L. L. Baggerly et al.

Vitamin D Supplement Doses and Serum 25-Hydroxyvitamin D in the Range Associated with Cancer Prevention.

Anticancer Res. 2011 February 2011; 312: 607-612.

BACKGROUND: Studies indicate that intake of vitamin D in the range from 1,100 to 4,000 IU/d and a serum 25-hydroxyvitamin D concentration [25(OH)D] from 60-80 ng/ml may be needed to reduce cancer risk. Few community-based studies allow estimation of the dose-response relationship between oral intake of vitamin D and corresponding serum 25(OH)D in the range above 1,000 IU/d. **MATERIALS AND METHODS:** A descriptive study of serum 25(OH)D concentration and self-reported vitamin D intake in a community-based cohort ($n=3,667$, mean age 51.3 ± 13.4 y).

RESULTS: Serum 25(OH)D rose as a function of self-reported vitamin D supplement ingestion in a curvilinear fashion, with no intakes of 10,000 IU/d or lower producing 25(OH)D values above the lower-bound of the zone of potential toxicity (200 ng/ml). Unsupplemented all-source input was estimated at 3,300 IU/d. The supplemental dose ensuring that 975% of this population achieved a serum 25(OH)D of at least 40 ng/ml was 9,600 IU/d.

CONCLUSION: Universal intake of up to 40,000 IU vitamin D per day is unlikely to result in vitamin D toxicity.

STUDY OF THE MONTH

Epstein, MM, J. L. Kasperzyk, O. Andren, et al.

Dietary Zinc and Prostate Cancer Survival in a Swedish Cohort.

Am J Clin Nutr. 2011 Mar; 933: 586-593.

BACKGROUND: Zinc is involved in many essential cellular functions, including DNA repair and immune system maintenance. Although experimental evidence supports a role for zinc in prostate carcinogenesis, epidemiologic data are inconsistent; no data on cancer-specific survival have been reported. **OBJECTIVE:** Our objective was to determine whether dietary zinc assessed near the time of prostate cancer diagnosis is associated with improved disease-specific survival. **DESIGN:** This population-based cohort consists of 525 men aged <80 y from Orebro County, Sweden, with a diagnosis of prostate cancer made between 1989 and 1994. Study participants completed self-administered food-frequency questionnaires, and zinc intake was derived from nutrient databases. Cox proportional hazards regression was used to estimate multivariate hazard ratios (HRs) and 95% CIs for time to death from prostate cancer as well as death from all causes through February 2009 by quartile (Q) of dietary zinc intake. Models were also stratified by disease stage at diagnosis (localized or advanced).

RESULTS: With a median follow-up of 6.4 y, 218 (42%) men died of prostate cancer and 257 (49%) died of other causes. High dietary zinc intake was associated with a reduced risk of prostate cancer-specific mortality (HR(Q4 vs Q1): 0.64; 95% CI: 0.44, 0.94; P for trend = 0.05) in the study population. The association was stronger in men with localized tumors (HR: 0.24; 95% CI: 0.09, 0.66; P for trend = 0.005). Zinc intake was not associated with mortality from other causes.

CONCLUSION: These results suggest that high dietary intake of zinc is associated with lower prostate cancer-specific mortality after diagnosis, particularly in men with localized disease.



"Not everything that counts can be counted, and not everything that can be counted counts."

- Albert Einstein



We are grateful to the Prostate Cancer Foundation BC and the Canadian Breast Cancer Foundation (BC/Yukon) for their generous support of *Research Updates*.



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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.

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