
Randomized Clinical Trial of Vitamin D3 Doses on Prostatic Vitamin D Metabolite Levels and Ki67 Labeling in Prostate Cancer Patients.

J Clin Endocrinol Metab. 2013 April 2013; 984: 1498-1507.

CONTEXT: Vitamin D3 might benefit prostate cancer (PCa) patients because prostate cells can locally synthesize the active hormone calcitriol. OBJECTIVE: Our objective was to determine the effects of oral vitamin D3 on vitamin D metabolites and PCa proliferative activity in prostate tissue. DESIGN AND SETTING: We conducted a double-blind randomized clinical trial at surgical oncology clinics in Toronto, Canada. Patients: PCa patients (Gleason 6 or 7) participated in the study. Of 66 subjects who were enrolled, 63 completed the dosing protocol. INTERVENTION: Vitamin D3 (400, 10 000, or 40 000 IU/d) was orally administered before radical prostatectomy. MAIN OUTCOME MEASURES: We evaluated vitamin D metabolite levels and Ki67 labeling in surgical prostate tissue. Safety measures, PTH, and prostate-specific antigen (PSA) were also assessed. RESULTS: Prostate tissue and serum levels of vitamin D metabolites, including calcitriol, increased dose dependently (P < .03) and were significantly higher in the 40 000-IU/d group than in every other dose group (P < .03). Prostate vitamin D metabolites correlated positively with serum levels (P < .0001). Ki67 measures did not differ significantly among vitamin D dose groups. However, cross-sectional analysis indicated that the calcitriol level attained in prostate was inversely associated with Ki67 intensity and Ki67 (3+) percent positive nuclei in PCa and benign tissue (P < .05). Safety measures did not change adversely with dosing. Compared with the 400-IU/d group, serum PTH and PSA were lower in the combined higher-dose groups at the end of the study (P < .02). CONCLUSIONS: Oral vitamin D3 raised prostate calcitriol levels (level 1 evidence) and modestly lowered both PSA and PTH. Although Ki67 expression did not differ among dose groups, its levels correlated inversely with prostate calcitriol. These suggestions of clinical benefit justify continued clinical research.

INSPIREHEALTH'S INTERPRETATION: In this double-blind randomized clinical trial, higher doses of oral vitamin D (10,000 or 40,000 IU/d, rather than 400 IU/d) given to patients before radical prostatectomy significantly decreased PSA (prostate-specific antigen), a biomarker of cancer progression.
BREAST CANCER

Jagielski, CH, S. T. Hawley, K. Corbin, et al.

A Phoenix Rising: Who Considers Herself a “Survivor” After a Diagnosis of Breast Cancer?


PURPOSE: The purpose of this study is to investigate factors associated with patients’ identification of themselves as survivors after a diagnosis of breast cancer. METHODS: A self-administered survey was deployed through the nonprofit organization Breastcancer.org. As part of a larger study, we collected data on treatment, mental health, perceived prognosis, concerns about recurrence, and the question, “Do you consider yourself a survivor of breast cancer?” RESULTS: Of the 629 survey respondents, 492 (78%) considered themselves survivors of breast cancer. Factors independently associated with an affirmative response were (1) believing that one’s prognosis was “very good” compared to others (p = <0.001), (2) recalling being told that treatment was curative (p = 0.04), (3) having better mental health (p = 0.002), and (4) having received chemotherapy (p = 0.01). CONCLUSIONS AND IMPLICATIONS FOR CANCER SURVIVORS: The disparate factors associated with the identification of oneself as a survivor—both the perception of having a very good prognosis and having received chemotherapy (reflecting high-risk disease rather than a good prognosis) are intriguing. Clinicians caring for women with breast cancer should be sensitive to the fact that not everyone considers herself a survivor. Addressing transitions at the end of treatment and during the follow-up period may be challenging for clinicians and patients alike. Awareness of the complexities of survivor identification may help clinicians in counseling their patients.

INSPIREHEALTH’S INTERPRETATION: In a self-administered survey that asked the question, “Do you consider yourself a survivor of breast cancer?” it was found that only 78% of them considered themselves survivors. This was partly due to the belief in a good prognosis, being told that the treatment was curative, having a better mental state and having received chemotherapy. This brought into question the need to address challenges in the transition between the end of treatment and the follow-up period, and the need to address complexities of survivor identification.

ACUPUNCTURE

Bokmand, S and H. Flyger.

Acupuncture Relieves Menopausal Discomfort in Breast Cancer Patients: A Prospective, Double Blinded, Randomized Study.


BACKGROUND: This study evaluates the effect of acupuncture on hot flashes and disturbed night sleep in patients treated for breast cancer. The effect of acupuncture was tested against a sham-acupuncture group and a no-treatment control group. Plasma estradiol was measured to rule out this as cause of effect. Side effects of the treatment were registered. METHODS: We randomized 94 women into the study: 31 had acupuncture, 29 had sham acupuncture and 34 had no treatment. FINDINGS: In the acupuncture group, 16 patients (52%) experienced a significant effect on hot flashes compared with seven patients (24%) in the sham group (p < 0.05). The effect came after the second acupuncture session and lasted for at least 12 weeks after last treatment. A statistically significant positive effect was seen on sleep in the acupuncture group compared with the sham-acupuncture and no-treatment groups. The effect was not correlated with increased levels of plasma estradiol. No side effects of acupuncture were registered. INTERPRETATION: We find that acupuncture significantly relieves hot flashes and sleep disturbances and is a good and safe treatment in women treated for breast cancer. The project is registered at ClinicalTrials.gov (no: NCT00425776).

INSPIREHEALTH’S INTERPRETATION: In this randomized controlled study, acupuncture safely relieved hot flashes and sleep disturbances in breast cancer patients for at least 12 weeks after the last acupuncture treatment.

ANTIOXIDANTS

Babaee, N, D. Moslemi, M. Khalilpour, et al.

Antioxidant Capacity of Calendula Officinalis Flowers Extract and Prevention of Radiation Induced Oropharyngeal Mucositis in Patients with Head and Neck Cancers: A Randomized Controlled Clinical Study.

Daru. 2013 Mar 7; 211: 18.

BACKGROUND: This study was designed to determine the effect of Calendula officinalis flowers extract mouthwash as oral gel on radiation-induced oropharyngeal mucositis (OM) in patients with head-and-neck cancer. METHODS: Forty patients with neck and head cancers under radiotherapy or concurrent chemoradiotherapy protocols were randomly assigned to receive either 2% calendula extract mouthwash or placebo (20 patients in each group). Patients were treated with telecobalt radiotherapy at conventional fractionation (200 cGy/fraction, five fractions weekly, 30-35 fractions within 4-7 weeks). The oropharyngeal mucositis was evaluated by two clinical investigators (a radiation oncologist and a dentist), using the oral mucositis assessment scale (OMAS). Trying to find out the possible mechanism of action of the treatment, total antioxidant, polyphenol and flavonoid
contents, and quercetin concentration of the mouth wash were measured. **RESULTS:** Calendula mouthwash significantly decreased the intensity of OM compared to placebo at week 2 (score: 5.5 vs. 6.8, p = 0.019), week 3 (score: 8.25 vs. 10.95, p < 0.0001) and week 6 (score: 11.4 vs. 13.35, p = 0.031). Total antioxidant, polyphenol and flavonoid contents and quercetin concentration of the 2% extract were 2353.4 ± 56.5 μM, 313.40 ± 6.52 mg/g, 76.66 ± 23.24 mg/g, and 19.41 ± 4.34 mg/l, respectively. **CONCLUSION:** Calendula extract gel could be effective on decreasing the intensity of radiotherapy-induced OM during the treatment and antioxidant capacity may be partly responsible for the effect.

**INSPIREHEALTH’S INTERPRETATION:** Patients with head and neck cancer who experience oral mucositis (inflammation and sores in the mouth) as a result of radiotherapy may benefit from 2% *Calendula officinalis* extract gel, and this might be partly due to the gel’s antioxidant properties.

**REFLEXOLOGY**

**Health-Related Quality-of-Life Outcomes: A Reflexology Trial with Patients with Advanced-Stage Breast Cancer.**

**PURPOSE/OBJECTIVES:** To evaluate the safety and efficacy of reflexology, a complementary therapy that applies pressure to specific areas of the body. **DESIGN:** Longitudinal, randomized clinical trial. **SETTING:** Thirteen community-based medical oncology clinics across the midwestern United States. **SAMPLE:** A convenience sample of 385 predominantly Caucasian women with advanced-stage breast cancer receiving chemotherapy and/or hormonal therapy. **METHODS:** Following the baseline interview, women were randomized into three primary groups: reflexology (n = 95), lay foot manipulation (LFM) (n = 95), or conventional care (n = 96). Two preliminary reflexology (n = 51) and LFM (n = 48) test groups were used to establish the protocols. Participants were interviewed again postintervention at study weeks 5 and 11. **MAIN RESEARCH VARIABLES:** Breast cancer-specific health-related quality of life (HRQOL), physical functioning, and symptoms. **FINDINGS:** No adverse events were reported. A longitudinal comparison revealed significant improvements in physical functioning for the reflexology group compared to the control group (p = 0.04). Severity of dyspnea was reduced in the reflexology group compared to the control group (p < 0.01) and the LFM group (p = 0.02). No differences were found on breast cancer-specific HRQOL, depressive symptomatology, state anxiety, pain, and nausea. **CONCLUSIONS:** Reflexology may be added to existing evidence-based supportive care to improve HRQOL for patients with advanced-stage breast cancer during chemotherapy and/or hormonal therapy. **IMPLICATIONS FOR NURSING:** Reflexology can be recommended for safety and usefulness in relieving dyspnea and enhancing functional status among women with advanced-stage breast cancer.

**INSPIREHEALTH’S INTERPRETATION:** In this randomized controlled study of primarily Caucasian women with advanced stage breast cancer, reflexology significantly improved physical functioning and decreased severity of dyspnea (difficulty in breathing).

**PROBIOTICS**

**A Systematic Review and Meta-Analysis of Probiotics for the Management of Radiation Induced Bowel Disease.**

**BACKGROUND & AIMS:** A meta-analysis to estimate the efficacy of probiotics in prevention of radiation-induced bowel disease after pelvic radiotherapy has been performed. Previous attempts have arguably failed to provide a comprehensive analysis of clinical trials and their outcomes. **METHODS:** We searched for studies indexed in Medline, EMBASE, Cochrane Library, and on-line clinical trials registers. There was no language or time limit. Each study was evaluated for methodological quality and outcomes. We identified four outcomes on which to perform meta-analysis: incidence of diarrhoea, loperamide use, watery, and soft stools (Bristol Stool Chart). Odds ratio (OR) was used to compare efficacy, and the pooled OR was estimated using a random effects model; heterogeneity was assessed with Cochran’s Q and Higgins I² test. Analyses were performed using Review Manager 5.2. **RESULTS:** Ten studies were included in our systematic review, of which six were subjected to meta-analysis to compare probiotics against placebo. Quality assessment showed an unclear risk due to incomplete outcome data and lack of performance of intention-to-treat analysis, while blinding and randomization issues were present in certain studies. Pooled results showed heterogeneity (Cochran’s Q: p < 0.05; I²: high). However the pooled OR for the incidence of diarrhoea, synthesized from 6 studies, significantly favoured the use of probiotics over control (OR = 0.44, 95% CI 0.21-0.92). Numerically, but not statistically, probiotics seem to decrease loperamide use (OR = 0.29, 95% CI 0.01-6.80) and the incidence of watery stools (OR = 0.36, 95% CI 0.05-2.81). **CONCLUSIONS:** In conclusion, probiotic supplementation shows a probable beneficial effect in the prevention, and possible benefit in the treatment, of radiation-induced diarrhoea.
**INSPIREHEALTH’S INTERPRETATION:** In this comprehensive review of studies to assess the effectiveness of probiotics in preventing and treating radiation-induced diarrhea, probiotics were found to decrease the use of the anti-diarrheal drug Loperamide and the incidence of watery stools.

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**EXERCISE**


**Too Sick Not to Exercise: Using a 6-Week, Home-Based Exercise Intervention for Cancer-Related Fatigue Self-Management for Postsurgical Non-Small Cell Lung Cancer Patients.**

*Cancer Nurs.* 2013 May-June; 363: 175-188.

**BACKGROUND:** Two prevalent unmet supportive care needs reported by the non-small cell lung cancer (NSCLC) population include the need to manage fatigue and attain adequate exercise to meet the physical demands of daily living. Yet, there are no guidelines for routine rehabilitative support to address fatigue and exercise for persons with NSCLC during the critical transition from hospital to home. **OBJECTIVE:** The objective of this study was to evaluate the feasibility, acceptability, safety, and changes in study end points of a home-based exercise intervention to enhance perceived self-efficacy for cancer-related fatigue (CRF) self-management for persons after thoracotomy for NSCLC transitioning from hospital to home. **INTERVENTIONS/METHODS:** Guided by the principles of the Transitional Care Model and the Theory of Symptom Self-management, a single-arm design composed of 7 participants with early-stage NSCLC performed light-intensity walking and balance exercises in a virtual reality environment with the Nintendo Wii Fit Plus. Exercise started the first week after hospitalization for thoracotomy and continued for 6 weeks. **RESULTS:** The intervention positively impacted end points such as CRF severity; perceived self-efficacy for fatigue self-management, walking, and balance; CRF self-management behaviors (walking and balance exercises); and functional performance (number of steps taken per day). **CONCLUSIONS:** A home-based, light-intensity exercise intervention for patients after thoracotomy for NSCLC is feasible, safe, well tolerated, and highly acceptable showing positive changes in CRF self-management. **IMPLICATIONS FOR PRACTICE:** Beginning evidence suggests that a light-intensity in-home walking and balance intervention after hospitalization for thoracotomy for NSCLC is a potentially effective rehabilitative CRF self-management intervention. Next steps include testing of this health-promoting self-management intervention in a larger-scale randomized controlled trial.

**INSPIREHEALTH’S INTERPRETATION:** A home-based, light-intensity exercise program (including walking and balance exercises) in a virtual reality environment is a safe and effective way of managing cancer-related fatigue in non-small cell lung cancer patients recovering from surgery.

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Mutrie, N. A. Campbell, S. Barry, et al.

**Five-Year Follow-Up of Participants in a Randomised Controlled Trial Showing Benefits from Exercise for Breast Cancer Survivors during Adjuvant Treatment. Are there Lasting Effects?**

*J Cancer Surviv.* 2012 Dec; 64: 420-430.

**PURPOSE:** In an earlier randomised controlled trial, we showed that early stage breast cancer patients who received a supervised exercise programme, with discussion of behaviour change techniques, had psychological and functional benefits 6 months after the intervention. The purpose of this study was to determine if benefits observed at 6 months persisted 18 and 60 months later. **METHODS:** Women who were in the original trial were contacted at 18 and 60 months after intervention. Original measures were repeated. **RESULTS:** Of the 148 women from the original study who agreed to be contacted again, 114 attended for follow-up at 18 months and 87 at 60 months. Women in the original intervention group reported more leisure time physical activity and more positive moods at 60 months than women in the original control group. Irrespective of original group allocation, women who were more active consistently reported lower levels of depression and increased quality of life compared to those who were less active. **CONCLUSIONS:** We have shown that there are lasting benefits to an exercise intervention delivered during treatment to breast cancer survivors. Regular activity should be encouraged for women with early stage breast cancer as this can have lasting implications for physical and psychological functioning.

**INSPIREHEALTH’S INTERPRETATION:** In this randomized controlled study with a 5-year follow-up, it was demonstrated that a supervised exercise program combined with a discussion of behavior change techniques delivered during treatment can have long-term benefits (reduced depression and increased quality of life) for breast cancer survivors.

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**E-VERSION EXTRA**

Walter, R. B., S. A. Buckley and E. White.

**Regular Recreational Physical Activity and Risk of Hematologic Malignancies: Results from the Prospective Vitamins and Lifestyle (Vital) Study.**


**BACKGROUND:** Conflicting evidence exists on the relationship between physical activity (PA) and incident hematologic malignancies. Herein, we used a large cohort study to examine this association. **PATIENTS AND METHODS:** 65,322 volunteers aged 50-76 years were recruited from 2000 to 2002. Incident hematologic malignancies (n = 666) were identified through 2009
by linkage to the Surveillance, Epidemiology, and End Results cancer registry. Hazard ratios (HRs) for hematologic malignancies associated with PA averaged over 10 years before baseline were estimated with Cox proportional hazards models, adjusting for factors associated with hematologic cancers or PA. **RESULTS:** There was a decreased risk of hematologic malignancies associated with PA (HR = 0.66 [95% confidence interval, 95% CI 0.51-0.86] for the highest tertile of all PA, P-trend = 0.005, and HR = 0.60 [95% CI 0.44-0.82] for the highest tertile of moderate/high-intensity PA, P-trend = 0.002). These associations were strongest for myeloid neoplasms (HR = 0.48 [95% CI 0.29-0.79] for the highest tertile of all PA, P-trend = 0.013, and HR = 0.40 [95% CI 0.21-0.77] for the highest tertile of moderate/high-intensity PA, P-trend = 0.016). There were also significant associations between PA and chronic lymphocytic leukemia/small lymphocytic lymphoma or other mature B-cell lymphomas except plasma cell disorders. **CONCLUSIONS:** Our study offers the strongest epidemiological evidence, to date, to suggest an association between regular PA and dose-dependent risk reduction for most hematologic malignancies, particularly myeloid neoplasms.

**INSPIREHEALTH’S INTERPRETATION:** Regular physical exercise (particularly moderate/high intensity exercise) may help prevent hematologic malignancies (cancer growths related to blood and bone marrow).

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**MEDITATION**

Lavretsky, H, E. S. Epel, P. Siddarth, et al.

**A pilot study of yogic meditation for family dementia caregivers with depressive symptoms: effects on mental health, cognition, and telomerase activity.**


**BACKGROUND:** This study examined the effects of brief daily yogic meditation on mental health, cognitive functioning, and immune cell telomerase activity in family dementia caregivers with mild depressive symptoms. **METHODS:** Thirty-nine family dementia caregivers (mean age 60.3 years old (SD = 10.2)) were randomized to practicing Kirtan Kriya or listening to relaxation music for 12 min per day for 8 weeks. The severity of depressive symptoms, mental and cognitive functioning were assessed at baseline and follow-up. Telomerase activity in peripheral blood mononuclear cells (PMBC) was examined in peripheral PBMC pre-intervention and post-intervention. **RESULTS:** The meditation group showed significantly lower levels of depressive symptoms and greater improvement in mental health and cognitive functioning compared with the relaxation group. In the meditation group, 65.2% showed 50% improvement on the Hamilton Depression Rating scale and 52% of the participants showed 50% improvement on the Mental Health Composite Summary score of the Short Form-36 scale compared with 31.2% and 19%, respectively, in the relaxation group (p < 0.05). The meditation group showed 43% improvement in telomerase activity compared with 3.7% in the relaxation group (p = 0.05). **CONCLUSION:** This pilot study found that brief daily meditation practices by family dementia caregivers can lead to improved mental and cognitive functioning and lower levels of depressive symptoms. This improvement is accompanied by an increase in telomerase activity suggesting improvement in stress-induced cellular aging. These results need to be confirmed in a larger sample.

**INSPIREHEALTH’S INTERPRETATION:** Brief daily yogic meditation effectively improved the mental health and cognitive functioning as well as stress-induced aging in family caregivers of dementia patients.

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**E-VERSION EXTRA**  **BELIEF IN GOD**

Rosmarin, DH, J. S. Bigda-Peyton, S. J. Kertz, et al.

**A Test of Faith in God and Treatment: The Relationship of Belief in God to psychiatric treatment outcomes.**

*J Affect Disord.* 2013 Apr 25; 1463: 441-446.

**BACKGROUND:** Belief in God is very common and tied to mental health/illness in the general population, yet its relevance to psychiatric patients has not been adequately studied. We examined relationships between belief in God and treatment outcomes, and identified mediating mechanisms. **METHODS:** We conducted a prospective study with n=159 patients in a day-treatment program at an academic psychiatric hospital. Belief in God, treatment credibility/expectancy, emotion regulation and congregational support were assessed prior to treatment. Primary outcomes were treatment response as well as degree of reduction in depression over treatment. Secondary outcomes were improvements in psychological well-being and reduction in self-harm. **RESULTS:** Belief in God was significantly higher among treatment responders than non-responders F(1,114)=4.81, p<.05. Higher levels of belief were also associated with greater reductions in depression (r=.21, p<.05) and self-harm (r=.24, p<.01), and greater improvements in psychological well-being (r=.19, p<.05) over course of treatment. Belief remained correlated with changes in depression and self-harm after controlling for age and gender. Perceived treatment credibility/expectancy, but not emotional regulation or community support, mediated relationships between belief in God and reductions in depression. No variables mediated relationships to other outcomes. Religious affiliation was also associated with treatment credibility/expectancy but not treatment outcomes. **CONCLUSIONS:** Belief in God, but not religious affiliation, was associated with better treatment outcomes. With respect to depression, this relationship was mediated by belief in the credibility of treatment and expectations for treatment gains.

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**RESEARCH UPDATES JULY 2013**
INSPIREHEALTH’S INTERPRETATION: In this Harvard Medical School study of psychiatric patients, belief in God but not religious affiliation was significantly associated with better treatment outcomes, greater reductions in depression and self-harm, and improvements in psychological well-being, regardless of age or gender. These findings could be applicable to cancer patients who experience mental health issues.

STUDY OF THE MONTH


Identifying Gender-Preferred Communication Styles within Online Cancer Communities: A Retrospective, Longitudinal Analysis.


BACKGROUND: The goal of this research is to determine if different gender-preferred social styles can be observed within the user interactions at an online cancer community. To achieve this goal, we identify and measure variables that pertain to each gender-specific social style. METHODS AND FINDINGS: We perform social network and statistical analysis on the communication flow of 8,388 members at six different cancer forums over eight years. Kruskal-Wallis tests were conducted to measure the difference between the number of intimate (and highly intimate) dyads, relationship length, and number of communications. We determine that two patients are more likely to form an intimate bond on a gender-specific cancer forum (ovarian P=<0.0001, breast P=0.0089, prostate P=0.0021). Two female patients are more likely to form a highly intimate bond on a female-specific cancer forum (Ovarian P<0.0001, Breast P<0.01). Typically a male patient communicates with more members than a female patient (Ovarian forum P=0.0406, Breast forum P=0.0013). A relationship between two patients is longer on the gender-specific cancer forums than a connection between two members not identified as patients (ovarian forum P=0.00406, breast forum P=0.00013, prostate forum P=0.0003).

CONCLUSION: The high level of interconnectedness among the prostate patients supports the hypothesis that men prefer to socialize in large, interconnected, less-intimate groups. A female patient is more likely to form a highly intimate connection with another female patient; this finding is consistent with the hypothesis that women prefer fewer, more intimate connections. The relationships of same-gender cancer patients last longer than other relationships; this finding demonstrates homophily within these online communities. Our findings regarding online communication preferences are in agreement with research findings from person-to-person communication preference studies. These findings should be considered when designing online communities as well as designing and evaluating psychosocial and educational interventions for cancer patients.

INSPIREHEALTH’S INTERPRETATION: Based on a study of gender-specific communication styles within online cancer forums, the researchers found that men prefer to communicate in larger, less intimate groups, while women tend to form fewer, more intimate bonds; also, same-gender cancer patients tend to form bonds that last longer than other relationships. These findings can inform the design of online support communities as well as psychosocial/educational programs for cancer patients.

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

InspireHealth provides patients with the knowledge, tools, and services to support their overall health during and after cancer treatment. Our medical doctors value conventional cancer treatments such as chemotherapy, radiation, and surgery. At the same time, they recognize the importance of supporting health, immune function, body, mind, and spirit.

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

InspireHealth’s Research Updates are compiled by Jan Rennie and Dr. Cletus D’Souza, PhD—with guidance from the editorial board—using InspireHealth’s Research Information System, a unique integrative cancer care knowledge management database. The editorial team selects authoritative articles based on their evidence and their relevance to this area of medicine. The editorial board includes: Dr. Hal Gunn, CEO and Co-founder, Dr. Janice Wright, Dr. Teresa Clarke, Dr. Ron Puhky, and Dr. Walter Lemmo, ND. For more information, email library@inspirehealth.ca