



# RESEARCH UPDATES

For the latest in worldwide integrated cancer care

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**InspireHealth**  
INTEGRATED CANCER CARE

## In this issue

### Cancer

Breast	1
Prostate	2
Colorectal	2
Endometrial	2
Gastric	3

### Therapies

Psychosocial	3
Nutrition	3
Supplements	4

### CAM of the Month

4

*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

Banerjee B, Vadiraj HS, Ram A, et al. **Effects of an integrated yoga program in modulating psychological stress and radiation-induced genotoxic stress in breast cancer patients undergoing radiotherapy.** *Integrative Cancer Therapies.* 2007 Sep;6(3):242-250.

Effects of an integrated yoga program in modulating perceived stress levels, anxiety, as well as depression levels and radiation-induced DNA damage were studied in 68 breast cancer patients undergoing radiotherapy. Two psychological questionnaires--Hospital Anxiety and Depression Scale (HADS) and Perceived Stress Scale (PSS)--and DNA damage assay were used in the study. There was a significant decrease in the HADS scores in the yoga intervention group, whereas the control group displayed an increase in these scores. Mean PSS was decreased in the yoga group, whereas the control group did not show any change pre- and postradiotherapy. Radiation-induced DNA damage was significantly elevated in both the yoga and control groups after radiotherapy, but the postradiotherapy DNA damage in the yoga group was slightly less when compared to the control group. An integrated approach of yoga intervention modulates the stress and DNA damage levels in breast cancer patients during radiotherapy.

Brisson J, Berube S, Diorio C, et al.

**Synchronized seasonal variations of mammographic breast density and plasma 25-hydroxyvitamin d.** *Cancer Epidemiology, Biomarkers & Prevention.* 2007 May;16(5):929-933.

BACKGROUND: Dietary vitamin D has been associated with lower mammographic breast density, a strong biomarker for breast cancer risk. Blood 25-hydroxyvitamin D [25(OH)D] is an integrated measure of vitamin D status (from food, supplements, and sun exposure) and varies with season. Our objective was to assess seasonal variations of breast density and compare such variations, if any, with that of 25(OH)D. METHODS: This cross-sectional study includes 741 premenopausal women recruited at screening mammography. Plasma 25(OH)D at recruitment was measured by RIA. Breast density was evaluated using a computer-assisted method. Seasonal variations were modeled using multivariate linear

regression and semi-parametric cubic smoothing splines. RESULTS: Season was strongly associated with 25(OH)D ( $P < 0.0001$ ). The highest smoothed mean 25(OH)D levels were seen at the end of July (81.5 nmol/L) and the lowest in mid-April (52.4 nmol/L). Breast density showed modest seasonal variations ( $P = 0.028$ ). The lowest smoothed mean breast density was observed in early December (38.5%) and the highest at the beginning of April (44.3%). When a 4-month lag time was presumed, seasonal variations of breast density appeared to be a mirror image of those of 25(OH)D, and the correlation of daily smoothed estimates of mean breast density and 25(OH)D was negative and strong ( $r = -0.90$ ). CONCLUSION: In premenopausal women, changes in blood vitamin D seem to be inversely related to changes in breast density with a lag time of about 4 months. This finding encourages further investigation of the possibility that vitamin D could reduce breast density and breast cancer risk.

Mattsson-Lidsle, B, B. Snickars-Von Wright, L. Lindholm and L. Fagerstrom. **Drama as a New Rehabilitation Possibility for Women Afflicted with Breast Cancer.** *Cancer Nurs.* 2007Dec;306:479-487.

The aim of this qualitative longitudinal study was to evaluate drama as a method within the rehabilitation of women afflicted with breast cancer. By purposeful sampling, 11 of a total of 20 women participated in the study and were interviewed 3 times over 9 months. The interviews were transcribed. The data analysis was an inductive latent content analysis. The results show that the women felt that their lives were out of balance before the drama exercises; the female and physical dimension was emphasized. During the drama exercises, it became apparent that breast cancer was a unifying factor; the women were able to share difficult experiences with each other. After the drama group, it appeared that the women's joy of living had returned, as well as better self-confidence, inner peace, and feelings of good health. During group meetings, the women experienced drama, support, and solidarity within a closed group. Important events in their lives were revealed, and the women were given an opportunity to confront their hidden thoughts and feelings and to express them. All the women felt support and solidarity within the group as well as a personal development.

Drama can be seen as a suitable rehabilitation method for women with breast cancer.

Shaw C, Mortimer P, Judd PA. **A randomized controlled trial of weight reduction as a treatment for breast cancer-related lymphedema.** *Cancer.* 2007 15 Oct;110(8):1868-1874. **BACKGROUND.** Obesity is considered a risk factor for the development of breast cancer-related lymphedema of the arm and as a poor prognostic factor in response to lymphedema treatment. The objective of this study was to examine weight reduction as a treatment for breast cancer-related lymphedema. **METHODS.** Twenty-one women with breast cancer-related lymphedema were randomized either to receive dietary advice for weight reduction or to receive a booklet on general healthy eating. They were monitored for 12 weeks. **RESULTS.** The primary outcome measure was arm volume at 12 weeks. The results indicated a significant reduction in swollen arm volume at the end of the 12-week period ( $P = .003$ ) in the intervention weight-reduction group. There was a significant reduction in body weight ( $P = .02$ ) and body mass index ( $P = .016$ ) in the weight-reduction group at the end of the 12-week study period. **CONCLUSIONS.** Weight loss achieved by dietary advice to reduce energy intake can reduce breast cancer-related lymphedema significantly.

## Prostate

Adhami VM, Mukhtar H. **Anti-oxidants from green tea and pomegranate for chemoprevention of prostate cancer.** *Mol Biotechnol.* 2007 Sep;37(1):52-57.

Among males, prostate cancer has become the second leading cause of cancer-related deaths in North America, with similar trends in many Western and developing countries. One way to control prostate cancer is through chemoprevention, which refers to the administration of synthetic or naturally occurring agents to block, reverse, or delay the process of carcinogenesis. For a variety of reasons, the most important of which is human acceptance, for chemopreventive intervention, naturally occurring diet-based agents are preferred. Prostate cancer is an ideal candidate disease for chemopreventive intervention, because it grows very slowly, likely for decades, before symptoms arise and a diagnosis is finally established, it has a long latency period, and it is typically diagnosed in men  $>50$  years of age. Most chemopreventive agents are antioxidant in nature. We have been defining the usefulness of dietary anti-oxidants for chemoprevention of prostate and other cancers. It is increasingly appreciated that some of these dietary anti-oxidants are nature's gift molecules endowed with cancer preventive and therapeutic properties. This review will focus on prostate cancer chemopreventive effects of polyphenolic anti-oxidants derived from green tea and pomegranate. It is a challenge to custom-tailor these gift molecules as cocktails in concentrations that can easily be consumed by humans for delaying prostate and other cancers. [References: 52].

Park, Y, P. N. Mitrou, V. Kipnis, A. Hollenbeck, A. Schatzkin and M. F. Leitzmann. **Calcium, Dairy Foods, and Risk of Incident and Fatal Prostate Cancer.** *Am J Epidemiol.* 2007 Dec; 16611: 1270-1279.

Calcium and dairy foods in relation to prostate cancer were examined in the National Institutes of Health (NIH)-AARP (formerly known as the American Association of Retired Persons) Diet and Health Study (1995/1996-2001). Diet was assessed with a food frequency questionnaire at baseline. Multivariate relative risks and 95% confidence intervals were estimated by Cox regression. During up to 6 years of follow-up ( $n = 293,888$ ), the authors identified 10,180 total prostate cancer cases (8,754 nonadvanced, 1,426 advanced, and 178 fatal cases). Total and supplemental calcium were unrelated to total and nonadvanced prostate cancer. However, a statistically nonsignificant positive association with total calcium was observed for advanced ([greater-than or equal

to]2,000 vs. 500- $_{\text{trend}} = 0.06$ ) and fatal ([greater-than or equal to]1,000 vs. 500- $_{\text{trend}} = 0.06$ ) and fatal ([greater-than or equal to]1,000 vs. 500- $_{\text{trend}} = 0.10$ ) prostate cancer. Skim milk, but not other dairy foods, was associated with increased risk of advanced prostate cancer ([greater-than or equal to]2 vs. zero servings/day: RR = 1.23, 95% CI: 0.99, 1.54;  $p_{\text{trend}} = 0.01$ ). In contrast, calcium from nondairy foods was associated with lower risk of nonadvanced prostate cancer ([greater-than or equal to]600 vs. = 0.01). In contrast, calcium from nondairy foods was associated with lower risk of nonadvanced prostate cancer ([greater-than or equal to]600 vs.  $_{\text{trend}} = 0.04$ ). Although the authors cannot definitively rule out a weak association for aggressive prostate cancer, their findings do not provide strong support for the hypothesis that calcium and dairy foods increase prostate cancer risk.



Thank you to the **BC Foundation for Prostate Disease** for their generous support.  
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## Colorectal

Martinez ME, Jacobs ET, Ashbeck EI, et al. **Meat intake, preparation methods, mutagens and colorectal adenoma recurrence.** *Carcinogenesis.* 2007 Sep;28(9):2019-2027. Red meat intake has been shown to be associated with higher risk of colorectal cancer. Though the exact mechanisms responsible for this association remain unknown, several tumorigenic properties of meat have been proposed. One well-supported biologic mechanism is elevated exposure to the genotoxic formation of heterocyclic amines (HCAs), which occur when meat is cooked at high temperatures for a long period of time. We prospectively assessed the relation between type of meat, meat preparation method, doneness, a metric of HCAs and other mutagens and colorectal adenoma recurrence among 869 participants in a chemoprevention trial of ursodeoxycholic acid. Unconditional logistic regression analyses were used to estimate odds ratios (ORs) and associated 95% confidence intervals (CIs). Most meat variables assessed were positively but weakly associated with recurrence of any adenoma. In contrast, recurrence of advanced or multiple adenomas was more strongly associated with a number of the meat exposure variables evaluated. For recurrence of advanced lesions, significant associations were detected among individuals in the highest when compared with the lowest tertile of intake for pan-fried red meat (OR = 1.85; 95% CI = 1.10-3.13) and well/very well done red meat (OR = 1.71; 95% CI = 1.02-2.86). Significant positive associations were shown for recurrence of multiple adenomas and the following variables: processed meat (OR=1.83; 95% CI = 1.10-3.04), pan-fried red meat (OR = 1.63; 95% CI = 1.01-2.61), well/very well done red meat (OR= 1.68; 95% CI = 1.03-2.74), 2-amino-3,4,8-trimethylimidazo [4,5- f]quinoxaline (OR=1.74; 95% CI = 1.07-2.82) and 2-amino-3, 8-dimethylimidazo[4,5-f]quinoxaline (OR = 1.68; 95% CI = 03-2.75). Our results support a meat mutagen exposure hypothesis as a potential mechanism for recurrence of clinically significant adenomatous polyps.

## Endometrial

Viswanathan, AN, S. E. Hankinson and E. S. Schernhammer. . **Night Shift Work and the Risk of Endometrial Cancer.** *Cancer Res.* 200701Nov;6721:10618-10622.

Melatonin has several oncostatic properties, including possible anti-estrogenic and anti-aromatase activity, and seems to be linked with fat metabolism. Night workers have lower levels of melatonin, which may predispose them to develop cancer. Endometrial cancer risk is influenced significantly by hormonal and metabolic factors; therefore, we hypothesize that night workers may have an increased risk of endometrial cancer. Of the 121,701 women

enrolled in a prospective cohort study, 53,487 women provided data on rotating night shift work in 1988 and were followed through on June 1, 2004. A total of 515 women developed medical record-confirmed invasive endometrial cancer. We used Cox regression models to calculate multivariate relative risks (MVRs), controlling for endometrial cancer risk factors. Women who worked 20+ years of rotating night shifts had a significantly increased risk of endometrial cancer [MVR, 1.47; 95% confidence interval (95% CI), 1.03-1.14]. In stratified analyses, obese women working rotating night shifts doubled their baseline risk of endometrial cancer (MVR, 2.09; 95% CI, 1.24-3.52) compared with obese women who did no night work, whereas a nonsignificant increase was seen among non-obese women (MVR, 1.07; 95% CI, 0.60-1.92). Women working rotating night shifts for a long duration have a significantly increased risk of endometrial cancer, particularly if they are obese. We speculate that this increased risk is attributable to the effects of melatonin on hormonal and metabolic factors. Our results add to growing literature that suggests women who work at night may benefit from cancer prevention strategies.

## Gastric

M AM, Pera G, Agudo A, et al. **Cereal fiber intake may reduce risk of gastric adenocarcinomas: The EPIC-EURGAST study.** *International Journal of Cancer.* 2007 Oct 1;121(7):1618-1623. Numerous case-control studies suggest dietary fiber may reduce risk of gastric cancer, but this has not been confirmed prospectively. A previous case-control study reported reduced risk of gastric cardia adenocarcinomas associated with cereal fiber, but not with fruit or vegetable fiber. To date, different food sources of fiber have not been examined with respect to noncardia tumors or diverse histologic sub-types. This study prospectively examines associations between fiber from different food sources and incident gastric adenocarcinomas (GC) among more than 435,000 subjects from 10 countries participating in the European Prospective Investigation into Cancer and Nutrition study. Subjects aged 25-70 years completed dietary questionnaires in 1992-98, and were followed up for a median of 6.7 years. About 312 incident GCs were observed. The relative risk of GC was estimated based on cohort-wide sex-specific fiber intake quartiles using proportional hazards models to estimate hazards ratios (HRs) and 95% confidence intervals (CIs). Intakes of cereal fiber, but not total, fruit or vegetable fiber, were associated with reduced GC risk [adjusted HR for the highest vs. lowest quartile of cereal fiber 0.69, 0.48-0.99]. There was a strong inverse association for diffuse [HR 0.43, 0.22-0.86], but not intestinal type [HR 0.98, 0.54-1.80] tumors. Associations for cardia vs. noncardia tumors were similar to those for overall GC, although cardia associations did not reach significance. Cereal fiber consumption may help to reduce risk of GC, particularly diffuse type tumors. Further study on different food sources of fiber in relation to GC risk is warranted to confirm these relationships.

## Psychosocial

Andersen BL, Farrar WB, Golden-Kreutz D, et al. **Distress reduction from a psychological intervention contributes to improved health for cancer patients.** *Brain, Behavior, & Immunity.* 2007 Oct; 21(7):953-961.

**PURPOSE:** Psychological interventions are efficacious in reducing emotional distress for cancer patients. However, it is not clear whether psychological improvements are, in turn, related to improved health. A clinical trial tests whether a psychological intervention for cancer patients can do so, and also tests two routes to achieve better health: (a) reducing patients' Emotional Distress, and/or (b) enhancing their functional immunity. **METHODS:** Post-surgery, 227 breast cancer patients were randomized to intervention or assessment only Study Arms. Conducted in small groups, intervention sessions were offered

weekly for 4 months and followed by monthly sessions for 8 months. Measures included psychological (distress), biological (immune), and health outcomes (performance status and evaluations of patient's symptomatology, including toxicity from cancer treatment, lab values) collected at baseline, 4 months, and 12 months. **RESULTS:** A path model revealed that intervention participation directly improved health ( $p < .05$ ) at 12 months. These effects remained when statistically controlling for baseline levels of distress, immunity, and health as well as sociodemographic, disease, and cancer treatment variables. Regarding the mechanisms for achieving better health, support was found for an indirect effect of distress reduction. That is, by specifically lowering intervention patients' distress at 4 months, their health was improved at 12 months ( $p < .05$ ). Although the intervention simultaneously improved patients' T-cell blastogenesis in response to phytohemagglutinin (PHA), the latter increases were unrelated to improved health. **CONCLUSION:** A convergence of biobehavioral effects and health improvements were observed. Behavioral change, rather than immunity change, was influential in achieving lower levels of symptomatology and higher functional status. Distress reduction is highlighted as an important mechanism by which health can be improved.

Shiple, BA, A. Weiss, G. Der, M. D. Taylor and I. J. Deary. . **Neuroticism, Extraversion, and Mortality in the UK Health and Lifestyle Survey: A 21-Year Prospective Cohort Study.** *Psychosom Med.* 2007 Nov; 69: 923-931. **OBJECTIVE:** To examine the influence of neuroticism and extraversion on all-cause and cause-specific mortality over 21 years after controlling for risk factors. **METHODS:** Participants were members of the Health and Lifestyle Survey, a British nationwide sample survey of 9003 adults. At baseline (1984 to 1985), individuals completed a sociodemographic and health questionnaire, underwent physical health examination, and completed the Eysenck Personality Inventory. Mortality was assessed for 21 years after baseline. A total of 5424 individuals had complete data. **RESULTS:** After controlling for age and gender, 1-standard deviation (SD) increase in neuroticism was related to 9% (hazard ratio (HR) = 1.09; 95% Confidence Interval (CI) = 1.03-1.16) increased risk of mortality from all causes. The association was nonsignificant (HR = 1.05; 95% CI = 0.99-1.11) after additionally controlling for occupational social class, education, smoking, alcohol consumption, physical activity, and health. There was 12% (HR = 1.12; 95% CI = 1.03-1.21) increased risk of death from cardiovascular disease associated with 1-SD increase in neuroticism. This was still significant after adjustment. When the sample was divided into 40- to 59-year-olds and those [greater-than or equal to]60 years, neuroticism remained a significant risk for all-cause mortality and cardiovascular disease mortality; associations were nonsignificant after controlling for all covariates. Neuroticism was not associated with deaths from stroke, respiratory disease, lung cancer, or other cancers. Extraversion was protective of death from respiratory disease (HR = 0.84; 95% CI = 0.70- 1.00). **CONCLUSIONS:** After controlling for several risk factors, high neuroticism was significantly related to risk of death from cardiovascular disease. The effects of neuroticism on death from cardiovascular disease may be mediated by sociodemographic, health behavior, and physiological factors.

## Nutrition

de Moreno de LeBlanc, A., C. Matar and G. Perdigon. . **The Application of Probiotics in Cancer.** *Br J Nutr.* 2007 Oct; 98: S105-S110.

Lactic acid bacteria (LAB) are present in many foods such as yoghurt and are frequently used as probiotics to favour some biological functions in the host. Many investigators have evaluated the therapeutic effects of yoghurt and LAB commonly used in yoghurt production against diseases such as cancer, infection, and

gastrointestinal disorders. The increase of immune cell activity in the prevention of cancer by LAB consumption has also been described. Another possible explanation for the preventive effect of probiotics on carcinogenesis is their effect on other bacteria in the intestine. Probiotics may suppress the growth of bacteria that convert procarcinogens into carcinogens, thereby reducing the amount of carcinogens in the intestine. The present review is focused on two types of cancer in which milk fermented by LAB may show a beneficial effect: colon cancer and breast cancer.

## Supplements

Block KI, Koch AC, Mead MN, et al. **Impact of antioxidant supplementation on chemotherapeutic efficacy: A systematic review of the evidence from randomized controlled trials.** *Cancer Treat Rev.*2007Aug;33(5):407-418.

**PURPOSE:** Much debate has arisen about whether antioxidant supplementation alters the efficacy of cancer chemotherapy. Some have argued that antioxidants scavenge the reactive oxygen species integral to the activity of certain chemotherapy drugs, thereby diminishing treatment efficacy. Others suggest antioxidants may mitigate toxicity and thus allow for uninterrupted treatment schedules and a reduced need for lowering chemotherapy doses. The objective of this study is to systematically review the literature in order to compile results from randomized trials that evaluate concurrent use of antioxidants with chemotherapy. **DESIGN:** MEDLINE, Cochrane, CinAhl, AMED, AltHealthWatch and EMBASE databases were searched. Only randomized, controlled clinical trials that reported survival and/or tumor response were included in the final tally. The literature searches were performed in duplicate following a standardized protocol. No meta-analysis was performed due to heterogeneity of tumor types and treatment protocols used in trials that met the inclusion criteria. **RESULTS:** Of 845 articles considered, 19 trials met the inclusion criteria. Antioxidants evaluated were: glutathione (7), melatonin (4), vitamin A (2), an antioxidant mixture (2), vitamin C (1), N-acetylcysteine (1), vitamin E (1) and ellagic acid (1). Subjects of most studies had advanced or relapsed disease. **CONCLUSION:** None of the trials reported evidence of significant decreases in efficacy from antioxidant supplementation during chemotherapy. Many of the studies indicated that antioxidant supplementation resulted in either increased survival times, increased tumor responses, or both, as well as fewer toxicities than controls; however, lack of adequate statistical power was a consistent limitation. Large, well-designed studies of antioxidant supplementation concurrent with chemotherapy are warranted. [References: 52].

Saller R, Romer-Luthi C, Brignoli R, et al. **A systematic review of the clinical significance of selenium.** *Schweizerische Zeitschrift Fur GanzheitsMedizin.*2007Oct;19(6):333-340.

**Background:** Selenium is an essential trace element and is contained in many foods, such as tomatoes, poultry, crustaceans, garlic and meat. Enzymes containing selenium counteract metabolic changes caused by endogenous and exogenous oxidative stress. In this way, selenium acts as an antioxidant. **Objective:** To conduct a systematic review of the clinical significance of selenium. **Methods:** Systematic analysis and evaluation of human studies - including prospective double-blind studies, epidemiological and retrospective studies, short term biochemical and haematological studies with surrogate markers - performed in the last 10 years and found in major electronic data bases, coupled to information in standard works and published monographs. **Results and Conclusion:** The symptoms of selenium deficiency may arise in severe chronic disease or from lack of selenium in the food. However, they are generally very rare. Subclinical selenium deficiency is thought to be frequent in countries with selenium-deficient soils or with imbalanced low selenium nutrition. The benefit of selenium (possibly in combination with zinc) in the prevention of infections or as an adjuvant in their treatment has not yet been confirmed. Studies on reducing the risk

of cancer with selenium have given encouraging results. Low selenium concentrations are probably correlated with increased risks of lung, prostate and intestinal cancer. Selenium supplements appear to be sensible for people under increased oxidative stress and for older patients at increased risk of infection. The nutritional societies of Germany, Austria and Switzerland (DACH recommendations) recommend 30-70 mug selenium per day for men and women. The maximal tolerated daily dose is estimated to be 400 mug. Daily doses of 900 mug selenium or more may be toxic.

## CAM of the Month

Verhoef, MJ, A. Mulkins, L. E. Carlson, R. J. Hilsden and A. Kania. **Assessing the Role of Evidence in Patients' Evaluation of Complementary Therapies: A Quality Study.** *Integrative Cancer Therapies.*2007Dec;64:345-353.

**Background:** Making the decision to use complementary and alternative medicine (CAM) for cancer treatment is difficult in light of the limited available evidence for these treatments. It is unclear how patients use evidence to make these decisions. **Objectives:** (1) Describe the type of information about CAM that cancer patients use in their decision making; (2) understand why certain types of information about CAM are accepted as evidence by cancer patients; and (3) explore the role of scientific evidence in treatment decision making. **Methods:** A qualitative study design using in-depth semistructured interviews with cancer patients attending 4 conventional and integrative health care institutions in Alberta and British Columbia, Canada, was used. **Results:** Twenty-seven patients were interviewed. Patients sought CAM information from a range of sources, including the Internet, health care providers, friends, relatives, and newspapers. Many expressed frustration about the overwhelming amount of available information and found it difficult to identify reliable information. Information was described as reliable if it supported them in arriving at a decision about CAM. Types of information participants identified included anecdotes, expert opinion, gut feeling, popular literature, scientific evidence, testimonials, advertising and trial and error. Profound differences were found between new CAM users, experienced CAM users, and users with late-stage cancer in type of information sought, the role of scientific evidence in decision making, and overall information needs. **Conclusion:** Although this was a relatively small qualitative study, the results suggest that (1) many patients do not value scientific evidence as highly as conventional providers and (2) it is important for clinicians and other information providers to be aware of the different types of information that patients seek out and access when making choices and decisions regarding CAM treatments and why they seek out these sources.

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.

Megan Wiebe, Clinical Librarian, compiles Research Updates under the supervision of the editorial board. She has a Master's degree in Library and Information Studies and a Bachelor's degree in Psychology from the University of British Columbia, and has worked in a variety of medical library settings. Megan can be contacted at [mwiebe@inspirehealth.ca](mailto:mwiebe@inspirehealth.ca) or 604-734-7125, ext 223.