



## RESEARCH UPDATES SPRING 2016

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### FOR THE LATEST IN WORLDWIDE SUPPORTIVE CANCER CARE

**IN THIS ISSUE:** Donovan et al. explore the potential psychological side effects of androgen deprivation therapy commonly used among prostate cancer patients. A paper by Tian and colleagues look at the effect of aerobic exercise on cancer-related fatigue. A review by Nea et al. highlights the unique lifestyle changes faced by shift workers with the subsequent possible effects on health. A study by Faghfoori and colleagues look at gut bacteria and its potential role in the prevention and treatment of colorectal cancer. Srednicka-Tober et al. compare the nutritional profiles of organic versus conventional dairy milk. In the Into the Vault study, Zebrack looks at the unique impact of a cancer diagnosis on adolescents and young adults.

## PROSTATE CANCER

Donovan, K.A., Walker, L.M., Wassersug, R.J., et al.

### Psychological effects of ADT on men with prostate cancer and their partners.

*Cancer* (2015); 121:4286-99.

**ABSTRACT |** The clinical benefits of androgen-deprivation therapy (ADT) for men with prostate cancer (PC) have been well documented and include living free from the symptoms of metastases for longer periods and improved quality of life. However, ADT comes with a host of its own serious side effects. There is considerable evidence of the adverse cardiovascular, metabolic, and musculoskeletal effects of ADT. Far less has been written about the psychological effects of ADT. This review highlights several adverse psychological effects of ADT. The authors provide evidence for the effect of ADT on men's sexual function, their partner, and their sexual relationship. Evidence of increased emotional lability and depressed mood in men who receive ADT is also presented, and the risk of depression in the patient's partner is discussed. The evidence for adverse cognitive effects with ADT is still emerging but suggests that ADT is associated with impairment in multiple cognitive domains. Finally, the available literature is reviewed on interventions to mitigate the psychological effects of ADT. Across the array of adverse effects, physical exercise appears to have the greatest potential to address the psychological effects of ADT both in men who are receiving ADT and in their partners.

**INSPIREHEALTH'S INTERPRETATION:** Androgen deprivation therapy (ADT) is a treatment commonly used among prostate cancer patients to help limit metastases. There are however, many known associated side effects. Much research has been conducted on the adverse physiological effects (e.g., cardiovascular, metabolic, musculoskeletal, etc.) of ADT but far less is known about the psychological effects. These psychological effects are quite significant and may include sexual impairment, loss of perceived masculinity, emotional dysfunction, depression, cognitive decline, and negative relationship effects with partners. Changes in sexual function may weigh heavily on both patients and their partners. Men undergoing ADT may experience heightened emotional expressions such as becoming spontaneously tearful, irritable, angry, or have increased sensitivity. Other side effects may include hot flashes, breast growth, loss of lean muscle mass, genital shrinkage, and weight gain around the hips. These side effects and changes to emotional behaviour may have an impact on a man's self-esteem, body image, and overall sense of identity. Depression among men who received ADT can be quite high, possibly due to persistently low testosterone levels. It is possible that a cascade of events may lead to depression. For example, hot flashes may magnify sleep problems, which may lead to insomnia, and then cause depression. Areas of the brain responsible for cognitive functioning such as memory, problem solving, spatial and verbal memory, coordinated visual perceptions and motor skills all have receptors for both androgens and estrogen.

Although further research in this area is needed, some studies suggest that between 47 and 69 percent of men receiving ADT may have impairment in at least one of these cognitive domains, possibly related to reduced levels of androgens available to

bind to specific brain nerve cells. Some of these side effects may also affect spousal relationships. Depending on the severity of psychological effects, interventions may include education, relationship counseling, psychosocial interventions, medication, and exercise. The authors highlight that exercise is associated with the greatest reduction in both psychological and physiological symptoms for both patients and partners. InspireHealth offers supportive care that may improve psychological side effects via exercise, counseling, and stress management programs.

## AEROBIC EXERCISE

Tian, L., Lu, H.J., Lin, L., & Hu, Y.

### Effects of aerobic exercise on cancer-related fatigue: a meta-analysis of randomized controlled trials.

*Supportive Care in Cancer* (2016), 24: 969–983.

**ABSTRACT | Background:** Cancer-related fatigue (CRF) is the most commonly reported and most distressing symptom in cancer patients. Currently, there are no effective strategies for managing this condition. **Objective:** The purpose of this study is to compare the effects of aerobic exercise on CRF with the standard of care. **Methods:** A systematic search for randomized controlled trials (RCTs) was performed using the Cochrane Library, JBI Library, Embase, MEDLINE, Web of Science, China Biology Medicine (CBM), and China National Knowledge Infrastructure (CNKI). The risk of bias was critically evaluated, and data were independently extracted by two reviewers. All of the analyses were performed using Review Manager 5. **Results:** A total of 26 qualified studies that included 2830 participants (aerobic exercise, 1426; control, 1404) were included in the meta-analysis. Cancer patients who completed adjuvant therapy in the aerobic exercise group reported reduced CRF levels relative to patients undergoing the standard of care. Aerobic exercise had a moderate effect on CRF for patients not currently undergoing anticancer treatment. Supervised aerobic exercise, exercise for 20–30 min/session, or exercise three times/week had a small effect on CRF. Exercise for 50 min/session or exercise two sessions/week had a significant effect on patient CRF, whereas 8 weeks of exercise had a moderate effect. **Conclusions:** Aerobic exercise is effective for the management of CRF, especially for patients who have completed adjuvant therapy. **Implications for practice:** Cancer patients can make more informed choices regarding their cancer-related fatigue management based on the best available evidence.

**INSPIREHEALTH'S INTERPRETATION:** Cancer-related fatigue is often characterized as fatigue that is not relieved by sleep or rest, does not result from physical exertion, and has a sudden onset. The authors of this paper searched the scientific literature and pooled data from all studies that investigated the effect of aerobic exercise on cancer-related fatigue using a randomized controlled trial research design. A total of 26 studies and 2830 participants was included in this meta-analysis. After pooling the studies of all types of cancer, aerobic exercise had a statistically significant effect on improving fatigue among participants. There was insufficient data to measure the effect of aerobic exercise on specific types of cancers other than for breast and nasopharyngeal carcinoma, which had nonsignificant and significant effects respectively. The nonsignificant effect of aerobic exercise on cancer-related fatigue for those with breast cancer is counter to what has been published in previously conducted meta-analyses, which had shown significant reductions in fatigue. No specific type of aerobic exercise was found to be superior in reducing fatigue, although moderate intensity activity (heart rate and breathing rate both increase, but you can still carry on a conversation) was found to improve fatigue (whereas mild or vigorous activity did not). Supervised exercise programs elicited improvements to fatigue whereas home-based programs did not.

Though the evidence suggested that aerobic exercise was effective in reducing fatigue levels for patients who were not currently undergoing treatment, the results for those currently in standard treatment (chemotherapy and/or radiation) were not conclusive. The authors recommend that exercise should be an integral part of cancer care standards to manage cancer-related fatigue post-treatment and suggest that two to three 20-50 minute bouts of exercise per week may provide the greatest benefit. It is important to note that it may be necessary to gradually increase levels of activity to achieve these targets. Although engaging in aerobic exercise when experiencing fatigue may seem counterintuitive, progressing slowly and working at an appropriate intensity can help to mitigate fatigue. InspireHealth provides individualized supervised exercise programs in line with current recommendations.

## DIET AND LIFESTYLE

Nea, F.M., Kearney, J., Livingstone, B.E., et al.

### Dietary and lifestyle habits and the associated health risks in shift workers.

*Nutrition Research Reviews* (2015), 28, 143–166.

**ABSTRACT |** Traditionally only a small proportion of the workforce was engaged in shift work. Changing economic pressures have resulted in increased engagement in shift work, with approximately 17% of the workforce in Europe engaged in this work pattern. The present narrative review aimed to summarise the data on the effects of shift work on the diet, lifestyle and health of employees, while addressing the barriers to, and opportunities for, improving health among shift workers. Shift work can result in low-quality diet and irregular eating patterns. Adverse health behaviours are also reported; particularly increased smoking

and poor sleep patterns. These altered lifestyle habits, in conjunction with disruption to circadian rhythms, can create an unfavourable metabolic phenotype which facilitates the development and progression of chronic disease. Although the data are inconclusive due to issues such as poor study design and inadequate control for confounding factors; shift workers appear to be at increased mental and physical health risk, particularly with regard to non-communicable diseases. Information is lacking on the obstacles to leading a healthier lifestyle while working shifts, and where opportunities lie for intervention and health promotion among this group. In order to provide an informed evidence base to assist shift workers in overcoming associated occupational hazards, this gap must be addressed. This review highlights the unique nutritional issues faced by shift workers, and the subsequent effect on health. In societies already burdened with increased incidence of non-communicable chronic diseases, there is a clear need for education and behaviour change interventions among this group.

**INSPIREHEALTH'S INTERPRETATION:** This review summarizes several altered lifestyle habits among those who are engaged in shift work. The authors go a step further by offering some opportunities for healthier lifestyle. Although this study is not performed among cancer patients, shift work has been labelled as a carcinogen, and thus the information seems pertinent.

**Dietary intake:** Total caloric intake among shift workers is similar to day workers. However, shift workers tend to consume more saturated fat, less dietary fibre, and fewer essential micronutrients such as vitamins A, D, E, and zinc. Shift workers are likely consuming a more pro-inflammatory diet than day workers. Irregular eating patterns among shift workers may disrupt circadian rhythms, (i.e., the 24-hour biological clock) which may increase blood glucose and triglyceride levels and increase the risk of type 2 diabetes and metabolic syndrome. **Physical activity:** The evidence relating physical activity and shift work has been quite mixed. It may be difficult for shift workers to participate in regular physical activity such as playing sports or attending exercise programs because of inconsistent schedules. Some studies have found that shift workers may engage in a higher level of physical activity during work hours than day workers but this is not conclusive. **Smoking:** Shift work, shifts longer than eight hours in length, or working 49-60 hours per week are all associated with higher smoking rates. Shift workers are more likely to take up smoking, are less likely to quit, and are more likely to have higher relapses than day workers. **Alcohol:** The literature relating alcohol consumption and shift work is mixed. On one hand, alcohol may be used to overcome sleeping difficulties. On the other hand, shift work interferes with family time and there may be a reduced opportunity for social alcohol consumption. **Sleep patterns:** Approximately 10-30% of shift workers report difficulty falling asleep, somnolence (sleepiness) during working hours that persists during days off, and shortened sleep duration. The shortest average sleep durations are measured among those working night shifts, rotating night shifts, and early morning shifts. Forward rotating shift schedules or slowly rotating shift patterns have the least negative impact on sleep length. There appears to be little difference between shift duration (i.e., 8 hours compared to 12 hours) on sleep patterns. **Health implications:** Circadian rhythm disruption may have systemic (body-wide) effects both physiologically and psychologically. Hormonal disruption, increased blood pressure, lower melatonin production, and adverse effects on metabolic markers, are all possible negative physiological effects of shift work. Psychologically, workers may experience increased work-related stress, lower quality of life, social isolation, and family conflict. The authors discuss at length the health implications of shift work on various conditions (e.g., cancer, obesity, metabolic syndrome, mental health), and conclude that shift work may have a negative impact on health. **Opportunities for a healthier lifestyle:** Weight loss, nutrition, and lifestyle education programs as well as health-promotion programs at work may provide opportunities for people to live healthier lives. Online support may also be effective. Additionally, health screening (e.g., for type 2 diabetes or cardiovascular disease) may identify employees with a greater need for lifestyle intervention.

## COLORECTAL CANCER

Faghfoori, Z., Gargari, B.P., Gharamaleki, A.S., et al.

### Cellular and molecular mechanisms of probiotics effects on colorectal cancer.

*Journal of Functional Foods* (2015), 18, 463–472.

**ABSTRACT |** Colorectal cancer is the most common malignancy of the gastrointestinal tract and it seems the colonic microbiota plays a significant role in the aetiology of colorectal cancer because it can influence many aspects of intestinal tract health including its physiology, metabolism, development, and immune homeostasis. Hence, all factors modulating the gut microflora and their metabolism are very interesting in cancer prevention. Probiotic bacteria have been examined for anti-cancer effects and different mechanisms were suggested about their antitumour functions. This study reviewed some of the possible cellular and molecular mechanisms of probiotics such as influencing intestinal microbial composition and pathogenic bacteria, the production of biological substance like short chain fatty acids and conjugated linoleic acid, inactivation of carcinogenic compounds especially those derived from food, improvement of intestinal barrier function, modulation of immune responses, apoptosis and anti-proliferative effects and antioxidant function.

**INSPIREHEALTH'S INTERPRETATION:** Interest in the roles that our gastrointestinal bacteria (the gut microbiome) play in our health and illness has been growing significantly. The human gastrointestinal (GI) tract contains tens of trillions of bacteria from approximately 1000 species. These bacterial microorganisms/microbes can influence our physiology, metabolism, immune system, and perhaps even our mood. Interestingly, about 2/3 of our gut microbiome is unique to each individual. Factors such as the food we eat, genetics, and the air we breathe can all influence the composition of our gut microbiome. Choosing a diet rich in a variety of whole foods and avoiding processed foods increases the number of bacterial species which is

thought to be related to increased health. Because colorectal cancer (CRC) is the third most common cancer worldwide, and because the gut microbiome is known to influence health in general, and colon health in particular, researchers are interested in understanding factors which support a healthy gut. It is generally accepted that the composition of the gut microbiome is quite different in those with colorectal cancer compared to healthy controls.

These authors reviewed the mechanisms by which probiotics may protect against the development of CRC. Because probiotic bacteria are “live microorganisms, that, when administered in adequate amounts, confer a health benefit on the host”, it is thought that ample intake of probiotic bacteria may favorably influence gut microbiome composition. Fermented foods such as live culture yogurt, sauerkraut, miso, kimchi, and kombucha all contain healthful probiotic bacteria species such as lactobacilli and bifidobacteria. Additionally, vegetables and fruits contain appropriate fibers and sugars to help the gut microbiome produce important vitamins. A healthy and diverse gut microbiome protects colon health by preventing overgrowth of pathogenic (disease causing) bacteria, extracting energy and nutrients from the diet, and optimizing immune function. In particular, probiotics can modify microbial composition in the gut to foster species which promote colon health by adhering to the GI mucosal lining to inhibit pathogen adhesion, and suppressing pathogen growth. Other beneficial mechanisms include production of anti-colon cancer compounds, maintenance of mucosal barrier integrity, ability to bind and eliminate mutagens (DNA mutations), enhanced immune function, inhibition of abnormal cell proliferation, and enhancement of cell apoptosis (programmed cell death). Importantly, there is no one strain that would give all these benefits, hence the need for a wide variety of bacterial species. The researchers conclude that large clinical trials need to be conducted to better establish the roles of probiotics in the prevention and possible treatment of CRC.

In the meantime, eating a mostly plant-based whole foods diet with a variety of fermented foods will maximize the chances of populating your gut with a healthy and diverse bacterial population. See also October 2014 and April/May 2015 editions of *Research Updates* for related reviews on the gut microbiome.

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## ORGANIC VS. CONVENTIONAL MILK

Srednicka-Tober, D., Baranski, M., Seal, C.J., et al.

### Higher PUFA and n-3 PUFA, conjugated linoleic acid, $\alpha$ -tocopherol and iron, but lower iodine and selenium concentrations in organic milk: a systematic literature review and meta- and redundancy analyses.

*British Journal of Nutrition* (2016), doi:10.1017/S0007114516000349.

**ABSTRACT** | Demand for organic milk is partially driven by consumer perceptions that it is more nutritious. However, there is still considerable uncertainty over whether the use of organic production standards affects milk quality. Here we report results of meta-analyses based on 170 published studies comparing the nutrient content of organic and conventional bovine milk. There were no significant differences in total SFA and MUFA concentrations between organic and conventional milk. However, concentrations of total PUFA and n-3 PUFA were significantly higher in organic milk, by an estimated 7 (95% CI -1, 15) % and 56 (95% CI 38, 74) %, respectively. Concentrations of  $\alpha$ -linolenic acid (ALA), very long-chain n-3 fatty acids (EPA + DPA + DHA) and conjugated linoleic acid were also significantly higher in organic milk, by an 69 (95% CI 53, 84) %, 57 (95% CI 27, 87)% and 41 (95% CI 14, 68) %, respectively. As there were no significant differences in total n-6 PUFA and linoleic acid (LA) concentrations, the n-6:n-3 and LA:ALA ratios were lower in organic milk, by an estimated 71 (95% CI -122, -20)% and 93 (95% CI -116, -70) %. It is concluded that organic bovine milk has a more desirable fatty acid composition than conventional milk. Meta analyses also showed that organic milk has significantly higher  $\alpha$ -tocopherol and Fe, but lower I and Se concentrations. Redundancy analysis of data from a large cross-European milk quality survey indicates that the higher grazing/conserved forage intakes in organic systems were the main reason for milk composition differences.

**INSPIREHEALTH'S INTERPRETATION:** The authors of this study examined the nutrient content of milk from organically-raised and conventionally-raised cows. They performed a meta-analysis of 170 studies, most of which were done in Europe. In order to statistically control for the wide variety of variables which could affect milk quality (other than organically- versus conventionally-raised), including cattle breed, farming practices, geographical location/soil chemistry, and type of study, the authors also conducted a redundancy analysis on the data from a large European milk quality study. Overall results indicated that milk from organic production systems had higher concentrations of healthy omega-3 fatty acids, particularly the healthy very long chain omega-3 fatty acids, with a resultant lowering of omega-6: omega-3 ratios thought to be important for anti-inflammatory effects. Organic milk also had higher concentrations of the antioxidant vitamins alpha-tocopherol (vitamin E) and carotenoids (vitamin A). Interestingly, these vitamin levels were higher in organic milk even though conventionally-raised dairy cattle are often given these vitamins as supplements. Although the minerals iodine and selenium levels were lower in organic milk, the levels fell well within the normal range. Additionally, there is some concern that higher concentrations of iodine from supplementation in conventionally-raised dairy cattle may be too high for optimal health. The redundancy analysis indicated that the nutritional differences were indeed related to higher grazing/forage intakes in the organically-raised cattle.

The authors concluded that a switch from conventional to organic production systems would result in significant nutritional

improvements particularly in the desirable long chain omega-3 fatty acid concentrations. Further studies examining the human health effects of consuming organic versus conventional milk would be an important next step. See also the June/July 2015 edition of *Research Updates* for a review on the fatty acid compositions of organically- versus conventionally-raised beef in Canada.

## INTO THE VAULT

Zebrack, B.J.

### Psychological, social, and behavioral issues for young adults with cancer.

*Cancer* (2011). 117 (10 suppl), 2289-2294.

**ABSTRACT** | Theories of human development suggest that, although all cancer patients experience a common set of life disruptions, they experience them differently, focus on different issues, and attach different levels of importance to different aspects of the experience depending on the time in life at which they were diagnosed. During the critical developmental transition from childhood to adulthood, older adolescents and young adults in particular have typical concerns with establishing identity, developing a positive body image and sexual identity, separating from parents, increasing involvement with peers and dating, and beginning to make decisions about careers or employment, higher education, and/or family. Accordingly, cancer-related issues such as premature confrontation with mortality, changes in physical appearance, increased dependence on parents, disruptions in social life and school/employment because of treatment, loss of reproductive capacity, and health-related concerns about the future may be particularly distressing for adolescents and young adults. Psychosocial and behavioral interventions for young adult cancer patients and survivors often involve assisting these individuals in retaining or returning to function in significant social roles, such as spouse, parent, student, worker, or friend. Successful interventions will enable these young people to overcome the detrimental impact of a health crisis and strengthen the internal and external coping resources available to them.

**INSPIREHEALTH'S INTERPRETATION:** In oncology, adolescents and young adults (ages 18-35) have been identified as a unique population, not only because of the types of cancer that are typically diagnosed in this age group (cancers prevalent among pediatric populations are far less common among adults and vice versa), but because of the lasting impact that a diagnosis at this age can have on quality of life and life expectancy. The purpose of this research paper was to highlight this unique population, and to discuss gaps in the current research, and in practical programs and interventions to support this population during a cancer diagnosis. The primary list of concerns outlined in this paper relate to premature confrontation with mortality, changes to physical appearance, body image and sexuality as a result of treatments, increased dependence on parents for financial support, changes to opportunity for education and employment resulting in changes to finances, changes to fertility and reproductive capacity over the long-term, and communication of a cancer diagnosis to younger children.

This paper discusses the vital importance of regaining a sense of control over one's life as part of the recovery process for adolescents and young adults. It is suggested that behavioural and psychosocial programs may enable adolescents and young adults to retain and return to functioning within their social roles (for example, as a spouse, parent, student, worker, friend), by optimizing coping mechanisms, support, and resources. This age group has identified the need to participate in programs with people of a similar age, concerns, and circumstances. Community programs exist for adolescents and young adults and as research continues to identify this population as one with a unique set a concerns, programs will continue to grow. There are local organizations offering support specifically to young adults. InspireHealth offers support groups, art therapy and other programs specifically for young adults and Young Adults Cancer Canada also offers regular programs and retreats.

**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 Rachel Mark, M.A. (kin)—with guidance from the editorial board—using InspireHealth's Research Information System, a unique supportive cancer care knowledge management database. The editorial board includes: Dr. Janice Wright, MD, CEO, Dr. Hannah Nette, MD, Dr. Lori McFarlane, MD, and Terry Heidt, M.Sc. For more information, email [library@inspirehealth.ca](mailto:library@inspirehealth.ca)

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