

ADT Study Newsletter

Quality of Life and Exercise Research

We are excited to bring you the third ADT newsletter for the Exercise and Bone Health studies! Thanks to the suggestions on the Study Survey you mailed in—this issue is a step up from the previous one. Four months have passed since the last issue, and more than just the weather has changed. Included in this newsletter are: updates on both studies, along with abstracts and summaries of some recent studies such as new treatments for prostate cancer. You can also read a testimonial from one of our home-based exercise study participants and their health coach. Dr. Maryam Hamidi, the research coordinator for the bone health study, returns with expert nutrition advice. You will also learn more about accelerometers from one of our co-investigators for the Exercise study, Dr. Catherine Sabiston. Finally, what would a health promotion-oriented study newsletter be without an exercise tip? Maria Habibelahian, a research student from York University, provides you with a functional exercise you can do anytime, anywhere.

Research Updates

Exercise Study

The purpose of this research study is to evaluate the effectiveness of 3 types of exercise program delivery methods for prostate cancer patients on hormone therapy (ADT) in order to determine which delivery type is the most effective and practical.

There are currently 51 participants (35 in Toronto and 16 in Calgary) enrolled in the exercise study. 22 Toronto participants have now completed their 6-month fitness assessment and are in the follow-up phase of the study, and 8 have now surpassed the 12-month mark. We are continuing to recruit, with plans to soon expand recruitment to Southlake Regional Health Centre in Newmarket.

Bone Health Study

While Androgen Deprivation Therapy (hormone therapy) or ADT helps treat prostate cancer, it can lead to bone loss and increase the risk of fractures. The purpose of this research study is to compare the effectiveness of two educational strategies which could help prostate cancer patients on ADT to improve their bone health.

A total of 119 men agreed to participate: 40 were randomized to receiving Building Strong Bones, an educational pamphlet, plus counseling by a Bone Health Care Coordinator; 40 were randomized to receiving Building Strong Bones plus their family physician was mailed an information package including the same pamphlet as well as the Canadian guidelines for bone health care. The remaining 39 men were randomized to receiving usual care by their regular health care team. At the time they completed the study these participants in the usual care group were offered an assessment in the Osteoporosis Clinic at UHN.



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We would like to thank Marcel Danesi for his wonderful contribution to our previous issue of the ADT Study Newsletter. Marcel wrote a testimonial titled, "Cancer in Body and Mind." The details that you have outlined about your experiences at ELLICSR and your journey are very much appreciated!

Transition from living healthy to a being a prostate cancer survivor

Author: Rene A. Araujo, Study Participant

While running several tests to find out the state of my prostate, I became aware of the potential to have cancer, this gave me time to understand and accept the outcome. With the help of my wife, my two kids and other family members I was able to overcome my sadness.

With the advice of the doctor, after being diagnosed I had surgery to have the prostate removed. But the cancer had spread out and the prostate was not removed,

therefore I was given radiation treatment and after that, hormone therapy.

My motivation to join the exercise study was to help researchers find their goals regarding prostate cancer. Being part of the exercise program helped me to understand the importance of maintaining my body in shape and confidence to fight the side effects of the treatment.

*I believe the innate desire to **be** and **feel** our best is a strong desire, mentally and physically...*

Author: Tina Changoor, Health Coach



We would like to thank
Prostate
Cancer Canada for
graciously
sponsoring the
Exercise study.

With that said, it's not uncommon to put personal health priorities at the end of our 'to do list'. Oftentimes, our work, relationships, and other activities take priority and this results in compromising on integrating physical activity in our daily schedule or getting enough sleep. For some, the day-to-day health sacrifices we make can add up. Sooner or later it can become quite challenging to feel encouraged and motivated in making health the important lifelong priority it should be.

As a health coach I help individuals prioritize their health by refocusing on everyday behaviours. By shifting the focus to *health* behaviours, it's possible to feel better and prevent illness. Being a health coach means actively engaging and collaborating with my clients on how healthy behaviours like regular physical activity, good nutrition, stress and relaxation techniques, and getting enough sleep can be readily done on an everyday basis. With the availability of smart-phone technology, I'm connected to clients 24 hours a day and together we co-monitor their health behaviours. Co-monitoring is an important component to health coaching because it provides practical understandings, and moment-to-moment insights, about the challenges and difficulties clients experience.

I joined the Prostate Cancer Survivorship Program (PCSP) as a health coach in 2014 with the goal of helping patients experience personal wellness and vitality by helping them make physical activity and other stress-reducing practices part of their daily lifestyle.

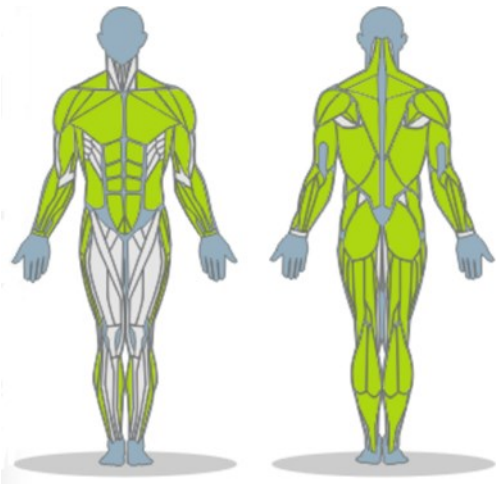
Since joining this program I have had the opportunity to work with individuals who come from diverse backgrounds but all share one thing in common, a desire to feel and be their personal best, day by day. I work with each client for 6 months and together we co-monitor and develop cognitive and behavioural strategies for implementing long-term healthy behavioural practices.

Clients are very generous when sharing their survivor experiences. Their experiences provide learning that would otherwise be impossible. It is a rich personal and professional experience to be health coaching such interesting and courageous individuals.



Exercise Tip

Author: Maria Habibelahian



Name of Exercise:

Walk-Out Plank

Target Muscle Groups:

This exercise is a whole body exercise with primary focus on the **abdominals, back, shoulders, and hamstrings**.

How to Complete this Exercise:

1. Start in a standing position; bend at the waist bringing your hands to the ground.
2. With only a slight a bend in the knees, place your hands on the ground shoulder width apart and slowly walk your hands forward coming up on the your toes until your body is parallel with the ground
3. Lower your hips to make you head neck and spine neutral. Pause.
4. Push your hips up and back, then slowly walk your hands back towards your feet returning yourself to the starting position.



Ready for a Challenge?

Once you are parallel with the ground, lower yourself down onto your elbows one arm at a time then push yourself back up.



Canadian Cancer Society
Société canadienne du cancer

Research Institute

We would like to thank the Canadian Cancer Society Research Institute for graciously sponsoring the Bone Health study.

Resistance Training for Higher Functioning in Cancer Patients

Although ADT is proven effective for treating prostate cancer, the side effects are known to reduce overall physical functioning that can ultimately hinder independence and the ability to carry out daily tasks.

In a recent study investigating the effects of resistance exercises amongst prostate cancer survivors, the researchers compared men in a supervised exercise program known as “POWIR” to a control group (FLEX) which performed a series of seated or lying whole-body stretches and relaxation exercise over 12 months. Both groups attended two classes a week and were responsible for one exercise session at home on their own. Those in the POWIR group performed resistance and impact training focusing on functional training like squats, pushups, and deadlifts, as well as using free weights rather than exercise machines to optimally challenge the muscles of body and have better carry over into day to day activities.

After 12 months, the study found both

types of training to be beneficial for improving physical function and reducing disability. Comparing the two groups, the POWIR group reported higher functioning and less bone loss compared to the FLEX group, and greater strength gains which were observed in as little as 6 months. Furthermore, members of the POWIR group observed greater strength gains in their legs, which may explain the lower rates of disability than in the FLEX group.

Interestingly, both groups saw similar improvements in walking speed. This shows that even though resistance training resulted in greater improvements, any increase in physical activity may be helpful for cancer patients. Therefore, the findings of this study show the importance of exercise programs, and the need for exercise prescriptions to become a routine component of cancer care. This makes our study even more relevant, as we try to find the best exercise delivery model to ensure the most people benefit in a feasible and resource-efficient way.

Original Article:

Resistance training reduces disability in prostate cancer survivors on androgen deprivation therapy: evidence from a randomized controlled trial

Reference:

Winters-Stone, K. M., Dobek, J. C., Bennett, J. A., Dieckmann, N. F., Maddalozzo, G. F., Ryan, C. W., & Beer, T. M. (2015). Resistance training reduces disability in prostate cancer survivors on androgen deprivation therapy: evidence from a randomized controlled trial. *Archives of Physical Medicine and Rehabilitation* 96(1), 7-14. doi: 10.1016/j.apmr.2014.08.010.



ADT with Radiotherapy vs. ADT alone for Prostate Cancer

In the Western Hemisphere, prostate cancer has been the most common cancer diagnosed in older men. For those with locally advanced prostate cancer – a state in which the cancerous cells have spread beyond the prostate gland capsule – either radiotherapy (RT) or androgen deprivation therapy (ADT/hormone therapy) are commonly used as treatment.

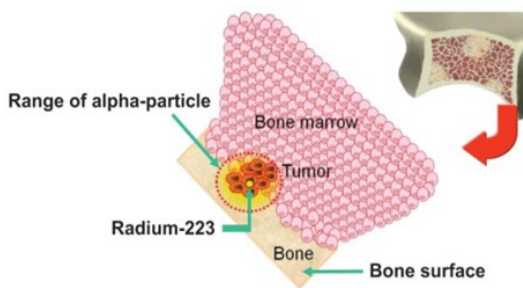
Some clinicians and scientists felt that ADT alone in this setting was as good as combining RT and ADT, but this was controversial. In a recent study, researchers followed 1205 men with locally advanced prostate cancer for 10 years who were randomly assigned to either receive RT and ADT or ADT alone. The results showed improved survival and slower disease progression among men receiving the combined treatment of RT and ADT compared to ADT alone. Short-term treatment side effects including hot flashes, impotence/libido, urinary frequency, and high blood pressure (hypertension) were fairly similar between the two groups, with no differences in cardiac problems. Bowel problems, however, were higher for those receiving both treatments. Most of these side effects were short-term and few men stopped treatment because of side effects.

Overall, the findings of this study confirm the benefits of combining radiotherapy with androgen deprivation therapy in men with locally advanced prostate cancer, and it firmly establishes its role as an effective treatment combination.

Reference: Mason, M. D., Parulekar, W. R., Sydes, M. R., Brundage, M., Kirkbride, P., Gospodarowicz, M., Cowan, R., Kostashuk, E. C., Anderson, J., Swanson, G., Parmar, M. K. B., Hayter, C., Jovic, G., Hiltz, A., Hetherington, J., Sathya, J. Barber, J. B. P., McKenzie, M., El-Sharkawi, S., Souhami, L., Hardman, P. D. J., Chen, B. E., & Warde, P. (2015). Final report of the intergroup randomized study of combined androgen-deprivation therapy plus radiotherapy versus androgen-deprivation therapy alone in locally advanced prostate cancer. *Journal of Clinical Oncology*. pii: JCO.2014.57.7510. [Epub ahead of print].

Radium-223 as a Novel Treatment for Prostate Cancer

Castration-resistant prostate cancer is defined as the further progression or recurrence of the disease despite the use of hormone therapy. As this happens, the cancer may spread to the bones (metastasis), putting the patient at a higher risk of various skeletal events such as bone fractures, worsening pain, and rarely spinal cord compression. Bone metastasis also increases the likelihood of needing some form of orthopedic surgery or radiation, which in turn can worsen the patient's health status and cause greater health care costs, reduced quality of life, and decreased survival. For men who become castrate-resistant, their prostate cancer specialist will often recommend new, more aggressive hormonal drugs such as Abiraterone or Enzalutamide, which further diminish bone health. Thus, the prevention of skeletal events is essential in the management of metastatic castration-resistance prostate cancer.



cancer cells since cancerous cells are more active than normal cells and therefore, more likely to pick up radium-223.

To determine the effectiveness and safety of treating men with castration-resistant cancer with radium-223 dichloride, Sartor et al. (2014) performed a randomized trial administering either radium-223 by intravenous infusion or a placebo every 4 weeks to participants in addition to their standard treatments. At the end of the trial, treatment with radium-223 was well received by the participants. The results showed no change in risk for bone fractures between the two groups. However, those receiving radium-223 experienced fewer skeletal events compared to the placebo group, and the skeletal events occurred much later. Radium-223 was also reported to decrease the risk of spinal cord compression and prolong survival. Therefore, radium-223 should be considered a good treatment option for men with castration-resistant prostate cancer with bone metastases. Radium-223 has recently been approved for use in Canada in specific patients with castration-resistant prostate cancer and metastases to bone.

Radium-223 dichloride uses high-energy alpha-particles, generating highly localized, intense radiation zones. It also mimics calcium, which naturally binds to a newly formed bone matrix. In this way, radium-223 gets to the parts of the bone where cancer is (metastases). It is an effective way to target bone

Original Article:

Effect of radium-223 dichloride on symptomatic skeletal events in patients with castration-resistant prostate cancer and bone metastases: results from a phase 3, double-blind, randomized trial

Reference:

Sartor, O., Coleman, R., Nilsson, S., Heinrich, D., Helle, S. I., O'Sullivan, J. M., Fossa, S. D., Chodacki, A., Weichno, P., Logue, J., Widmark, A., Johannessen, D. C., Hoskin, P., James, N. D., Solberg, A., Syndikus, I., Vogelzang, N. J., O'Bryan-Tear, C. G., Shan, M., Bruland, O. S., & Parker, C. (2014). Effect of radium-223 dichloride on symptomatic skeletal events in patients with castration-resistant prostate cancer and bone metastases: results from a phase 3, double-blind, randomized trial. *Lancet Oncology*, 15 (7), 738-46. doi: 10.1016/S1470-2045(14)70183-4.

ACTIVITY TIP:

Take the stairs instead of the elevator or escalator. As a fire and safety regulation, all buildings have stairs – use them! If you are in an apartment and you don't get out much, walk down the halls and stairs in your building.



Accelerometers

Author: Dr. Catherine Sabiston

WHAT IS THAT LITTLE RED DEVICE I HAVE TO WEAR AROUND MY WAIST?

In this study, we are interested in measuring physical activity the best way possible – which means using a questionnaire to ask you about your activity levels as well as asking you to wear that little red device around your waist. This device is called an accelerometer and it measures the movement that you make throughout the day. Accelerometers capture daily movement on a range of intensities by counting steps, allowing us to assess minutes of low to high intensity physical activity as well as sedentary behaviour (i.e., sitting or laying down) each day. Activity is measured in 30-second or 1-minute intervals to get a precise measure of activity throughout a 24-hour period.

ACTIVITY TIP:

Move up as much as possible throughout the day. There is new evidence that breaks in sedentary time are very important for health.

Stand during commercials while watching television (and even better, do some sit-ups or push-ups or, while sitting, try lifting your legs or rotating your legs as though you are on a bicycle).



WHY DO I NEED TO COMPLETE THE QUESTIONNAIRE AND WEAR THE ACCELEROMETER?

Questionnaires are self-report measures that are easy to administer and low-cost, but people sometimes forget or do not report some activities. Therefore, people tend to either over or under-report their physical activity. By combining the questionnaire with the accelerometer, we can learn what physical activity you are doing and see the amount and intensity of what you are doing. This gives the most accurate picture of your activity level and allows us to see if your level (i.e. sedentary, light, moderate, or vigorous) of physical activity is changing as a result throughout the study period and how this is affecting your health

WHAT IS DONE WITH THE DATA ONCE IT IS COLLECTED?

The data is used in a number of ways. First, we are able to examine each individual participant's physical activity patterns throughout the study. Second, we are able to compare questionnaire and accelerometer data to describe both purposeful and non-purposeful/subconscious physical activity levels. Third, we are able to compare the different measures across the different study groups to see if any of the strategies/programs are better for increasing different types and intensities of physical activity. This will ultimately help us to develop, test, and offer the best physical activity programs to meet the unique needs of men with prostate cancer.

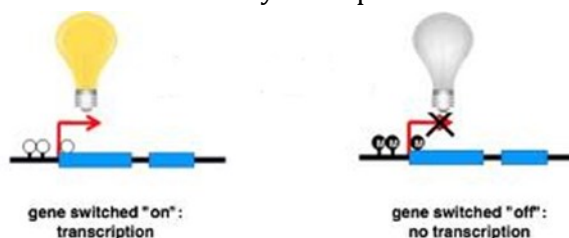
WHY IS ALL OF THIS IMPORTANT?

There is strong evidence that physical activity helps improve mental and physical health for men diagnosed with prostate cancer. However, little is known about the type, amount, and intensity of physical activity that is best for health benefits. In doing this study, and measuring physical activity as comprehensively as possible, we will be able to contribute to the research evidence on the benefits of physical activity as well as help to develop safe, cost-effective, and beneficial physical activity programs that could be delivered to the thousands of men diagnosed with prostate cancer each year in Canada.



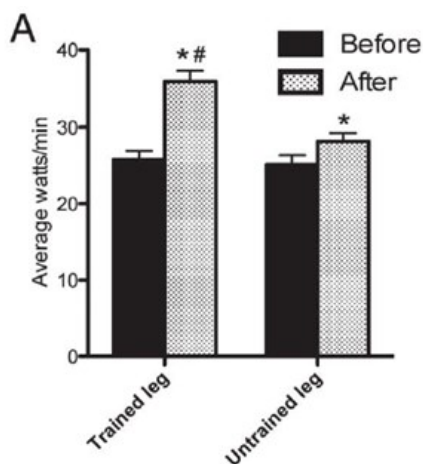
How exercise changes our DNA

We all know exercise enhances our physical fitness and overall health, what isn't really understood is exactly **how** does exercising translate into better health. The answer to this question may lie partly in our DNA. In the human genome, genes - which are responsible for physiological responses all over the body, are constantly turning on or off depending on what biochemical signals they receive. How much a given gene gets turned on or off in response to these signals is a result of a complex process known as "methylation", where clusters of atoms (methyl groups) attach to the outside of a gene, making them more or less able to receive and respond to the various signals from the body. It is well known that methylation patterns are influenced by our lifestyles like eating behaviors and environment, but not much has been explored around the long term effects of exercise.



At Karolinska University in Sweden, a group of researchers recruited young men and women to perform a supervised **one-legged knee-extension** exercise for 3 months (4x/week for 45 minutes). The idea behind using one leg was to ensure that any changes seen were a result of the exercise only and not other environmental factors.

By the end of the study, it was no surprise that each participant had one leg stronger than the other, but with further analysis of muscle tissue taken from both legs, over 5000 sites on the genome in the exercised leg featured new methylation patterns not seen in the non-exercised leg. Interestingly enough, the genes which saw the largest increases in methylation were genes responsible for muscle and glucose metabolism, whereas those responsible for control of inflammation, immunity, and gene copying saw the greatest decrease in methylation- essentially altering the genes that affect how healthy and fit our muscles are. This demonstrates that the changes in methylation were not random, but a controlled process likely from muscle adaptations to exercise.



Further research is needed to better understand these processes and the role of exercise, but the take-home message of these findings is that we **do** have the ability to influence our genes. Through exercise training, we have the ability to make ourselves healthier at the genome level and improve our quality of life.

Original Article:

An Integrative Analysis Reveals Coordinated Reprogramming of the Epigenome and the Transcriptome in Human Skeletal Muscle After Training

Reference:
Lindholm, M. E., Marabita, F., Gomez-Cabrero, D., Rundqvist, H., Ekstrom, T. J., Tegner, J., & Sundberg, C. J. (2014). An integrative analysis reveals coordinated reprogramming of epigenome and the transcriptome in human skeletal muscle after training. *Epigenetics*, 9(12), 1557-1569. doi: 10.4161/15592294.2014.982445.

Nutrition Tips from the Princess Margaret Prostate Center

Author: Maryam S. Hamidi, Ph.D.



Patients often ask if taking supplements would help improve their health. This is a good question but not an easy one to answer. Many studies have shown that taking supplements, in the absence of nutrient deficiencies, is not as effective in cancer prevention and treatment as healthy eating. Foods have a combination of nutrients that may work together to improve our health; whereas taking high doses of supplements without medical supervision can sometimes do more harm than good. **Advice to take supplements should only be given by someone who is directly involved in your medical care, as they are familiar with details of your medical condition, your medical history, medications you take, and treatments you are receiving.**

Supplements are needed when....

- ✓ A diet is low in a certain nutrient, or when nutrient deficiencies are detected. For example, a vitamin B12 supplement for vegans, or an iron supplement to help iron-deficiency anemia.
- ✓ Someone has an increased need for certain nutrients because of their medical condition or the medications they take. For example, 1000 international units (IU) of vitamin D supplements are currently recommended as a complementary therapy in men undergoing androgen deprivation therapy (ADT). Also, if men receiving ADT cannot meet their daily recommended intake of 1000-1200 mg of calcium from foods, calcium supplementation may be recommended.

Safety of low dose multivitamins/minerals

Most men can use a balanced multivitamin-mineral supplement safely, if the nutrients in it meet daily dosage guidelines. Safe multivitamins are those that do not contain more than 100% of the "Recommended Intake per day" of all nutrients. The total intake from all supplements should be lower than the "Tolerable UL Intake per day", unless your physician has advised you otherwise and is monitoring you. Examples of supplements are multivitamins, single supplements, combination products (e.g. bone health formula or meal replacements), and foods that are fortified with nutrients such as breakfast cereals, soy milk, rice milk, almond milk, and sports drinks. You can find the "Tolerable UL Intake per day" and the dosage guidelines for yourself based on your age, weight, height and physical activity level here: <http://fnic.nal.usda.gov/fnic/interactiveDRI/>

Potential problems or complications of taking dietary supplements without medical supervision:

♥ **Antioxidants, Vitamins: C, E, & Beta Carotene; Minerals: Selenium, Copper, & Zinc**

Studies which tested the use of antioxidant supplements to reduce the side effects of cancer treatment have shown that although those who took antioxidant supplements had fewer side effects from radiation therapy, they had more cancer recurrences later on. This suggests that antioxidant supplements taken **during** radiation therapy may decrease the effectiveness of radiation therapy and it is best to avoid taking them while receiving cancer treatment.

Furthermore...

- ◆ Long-term high doses of zinc (more than 40 mg/day) can cause the body's copper levels to drop, which may cause anemia and low white blood cell counts.
- ◆ Studies have shown that selenium supplements do not protect against prostate cancer, and may even cause adverse effects. Therefore, selenium supplements are not recommended.

Nutrition Tips from the Princess Margaret Prostate Center

Author: Maryam S. Hamidi, Ph.D.

♥ **Calcium**

High daily doses (higher than 1000 mg from supplements) can cause adverse effects. For men with prostate cancer, we advise against taking more than a total of 1200 mg of calcium per day from a combination of diet and supplements. You can measure your calcium intake here:

<http://osteconnections.azurewebsites.net/wp-content/uploads/2014/05/cat-onepage.pdf>

♥ **Vitamin A**

High daily doses (higher than 10,000 IU) may cause adverse reactions and can also increase the risk of bone fractures and certain cancers.

♥ **Vitamin B6**

High daily doses (higher than 100 mg) have been associated with pain, numbness in hands and legs, and trouble walking. A B-complex 100 multivitamin contains this amount.

♥ **Vitamin D**

High daily doses (higher than 4000 IU) can cause adverse reactions in some people. We advise against taking more than 2000 IU of vitamin D per day, unless your doctor has asked you to, and is monitoring your blood levels of vitamin D.

♥ **Folic Acid & B12**

There is no consensus regarding safety of folic acid supplements (doses higher than 400 mcg) and vitamin B12 (doses higher than 500 mcg) for men with prostate cancer. Therefore, high doses of folic acid and vitamin B12 are not recommended without medical supervision.

♥ **Omega Fatty Acids**

There is no consensus regarding the safety of omega-3 fatty acid supplements and flax seed oil for men with prostate cancer. Therefore, their uses are not recommended for men with prostate cancer.

♥ **Others**

- ♦ **St. John's wort:** May reduce the effectiveness of prescription drugs for heart disease, depression, seizures, certain cancers, or HIV.
- ♦ **Glucosamine & Glutamine:** Theoretically may reduce the effectiveness of Goselerin (Zoladex), a commonly used hormonal therapy for prostate cancer.
- ♦ **Dimethyl sulfoxide (DMSO):** may reduce effectiveness of Leuprolide (Lupron, Eligard) and Triptorelin (Trelstar), (two other common hormonal treatments for prostate cancer) as well as chemotherapy drugs such as cisplatin, carboplatin, and oxaliplatin.

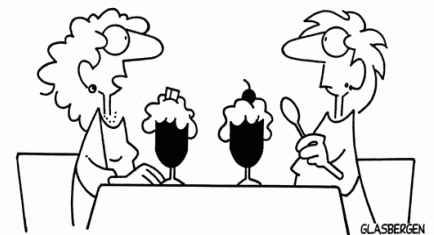
In closing, treat supplements like you treat your prescribed medications. A dietary supplement should not be the important part of your diet. Dietary supplements are intended to only supplement the diet when necessary. Be sure to also learn about the precautions or warnings of each supplement you are taking, as well as any side effects. For more information and nutrition and cancer related resources, you can visit the ADT Exercise Trial website at www.adtexercisetrial.ca!

Important tip

Before starting a new medication or supplement always inform your pharmacist which medications and supplements you are taking to make sure the combination is safe and to get the correct directions for usage



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"If you put a crouton on your sundae instead of a cherry, it counts as a salad."

Information about website

If you haven't taken a look at our website for the Exercise Study, please visit: www.adtexercisetrial.ca! You can now have easy access to all of the latest study updates, meet the study team, get links to useful resources on our website and much more!

You can also view and read our past newsletters through our website!

We always appreciate your help! If you'd like to support us and our research in prostate cancer, please visit our website and click on the '**Support Us**' link. Your generous donations/support will help Dr. Shabbir Alibhai and his team to continue research and educational efforts to improve the musculoskeletal health, quality of life, and function of men with prostate cancer.



If you have any suggestions about our newsletter or have any questions, please email Henriette at hbreunis@uhnresearch.ca or Holly at holly.stacey@uhn.ca. We'd love to hear from you!

ACTIVITY TIP:



If you have to drive, park the car as far away from your destination as possible. Instead of circling and waiting for the closest parking spot, drive to the furthest and emptiest part of the parking lot and walk

Meet the Team

We are very fortunate to have a very talented team working with us on both the Exercise and Bone Health studies. The principal investigator for both studies is **Dr. Shabbir Alibhai**.

Henriette Breunis, **Sara Durbano** and **Holly Stacey** are the research coordinators for the Bone Health and Exercise trials, respectively. **Darren Au** and **David Field** are working as outcome assessors for the exercise trial and **Meagan O'Neill** is the research assistant and Ph.D. student for the exercise study. **Joanna Sandoval** who has taken over for **Vikarnan Thiruvarooran** is the research student working on the exercise trial. In addition to these members, we also have **Dr. Maryam S. Hamidi**, the Bone Health Care Coordinator and **Maria Habibelahian**, a research student helping to deliver exercises. Finally, we welcome back **Mustafa Mohamedali** as a summer research student. Mustafa and Joanna will be analyzing our survey results. From all of our team we'd like to thank you for your continued participation and devotion to the studies.

