ALCOA
Active Living Coalition for Older Adults
CVAA
Coalition d'une vie active pour les aîné(e)s

Issue Number 12, September 2007

Research Update

Practical, leading edge research results applied to physical activity for older adults, in plain language for health practitioners and leaders.
Sponsored by the Active Living Coalition for Older Adults (ALCOA).

Physical Activity and Cancer: From Prevention to Recovery

Laurie Hoffman-Goetz, PhD, MPH - Department of Health Studies and Gerontology, University of Waterloo
Kerry S. Courneya, PhD - Faculty of Physical Education and Recreation, University of Alberta

Active Living Coalition for Older Adults

30 Delta Park Blvd.
Brampton, Ontario L6T 5E7
Toll-free: 800 549-9799
Tel.: 905 799-8490
Fax: 905 458-7422
E-mail: alcoa@ca.inter.net
www.alcoa.ca

Additional copies of ALCOA Research Update issues are available in print and electronic formats from the ALCOA office, or can be downloaded from www.alcoa.ca

The financial support of Health Canada is gratefully acknowledged.

ISBN 978-0-9685384-6-3

Who gets Cancer?

In Canada, cancer is mostly a disease of older adults. According to 2006 statistics from the Canadian Cancer Society, about 78% of all people with cancer and 81% of people who die of cancer are 60 and older. Many people with the most common cancers are also older adults. Seventy-nine percent (79%) of lung cancers, 52% of breast cancers, 81% of prostate cancers, and 78% of colorectal cancers are diagnosed in adults aged 60 years and over.

Fortunately, the chance of surviving cancer has steadily increased over the last few decades. This is because cancers are detected earlier, treatments are more effective, and supportive care is better. The most recent estimate is that 59% of people with invasive cancers will survive for five years. How long people survive varies dramatically. The difference is based on many factors including the type of cancer and how advanced the cancer was when it was diagnosed. However, older adults are less likely to survive some cancers. For example, 26% of people who are diagnosed with lung cancer before the age of 40 survive for five years after diagnosis but only 12% of those diagnosed after age 70 survive for five years. For the other common cancers, however, there are no clear connections between survival rates and a person's age when they are diagnosed with cancer. The high incidence and good survival rates have resulted in almost one-million Canadian cancer survivors. About 800,000 of these survivors are over the age of 60.

What is cancer?

Cancer is a descriptive term which covers more than one hundred diseases. Cancers can arise from any component of the body, and tumours starting in similar tissues may develop in very different ways. Despite these differences, all cancers share a number of fundamental characteristics. As Nobel Laureate Harold Varmus and National Medal of Science winner Robert Weinberg state, "cancer cells divide without restraint, cross boundaries they were meant to respect, and fail to display the characteristics of the cell lineage from which they were derived." Changes in how cells grow, develop, and communicate are controlled principally, but not exclusively, by genes. Cancer is a disease that develops because of how the genes act.

Acknowledgements

Authors:

Laurie Hoffman-Goetz, PhD, MPH

Kerry S. Corneya, PhD

ALCOA Research Committee Chair:

Michelle Porter, PhD
University of Manitoba
Winnipeg, MB

Research Committee Members:

Philippe Markon, PhD
University of Quebec
Chicoutimi, PQ

Sandy O'Brien Cousins, PhD
University of Alberta
Edmonton, AB

Gareth R. Jones, PhD
University of Western Ontario
London, ON

Mike Sharratt, PhD
University of Waterloo
Waterloo, ON

Anne Skuba
Older Adult Advisory Committee
ALCOA in Manitoba
Winnipeg, Manitoba

Reviewed by:

Gregory Videtic, MD, CM, FRCPC
Department of Radiation Oncologoy
Cleveland Clinic Foundation

Maria Chia, PhD
National Cancer Insitute of Canada

ALCOA Staff:

Patricia Clark

Photos:

Health Canada

Cancer is a process

When normal cells change into cancer cells, the process happens in three stages. During initiation, the cell's deoxyribonucleic acid (DNA) is damaged. Initiation can happen spontaneously or be triggered by carcinogens. The next stage is promotion, when more genetic changes take place. Promotion can include activating oncogenes, and activating or damaging tumour suppressor, caretaker and gatekeeper genes (see Table 1). During the promotion stage, cells can divide more rapidly or die less often than is normal. The final stage of cancer is progression, when cells proliferate uncontrollably, and normal cells lose their structure and can no longer function. Although researchers used to think that most cancers involved only a few genetic steps, we now know that cancer can involve many genetic changes.

Here are some key biological processes which are typical of cancer:

- cells lose sensitivity to signals that inhibit their growth
- cells do not die
- cells are able to divide endlessly
- new blood vessels develop to nourish the tumour

Can physical activity help prevent cancer?

Researchers have considered the relationship between physical activity and cancer prevention since 1922, when people observed that cancer mortality in men varied by occupation. Researchers hypothesized that the difference in mortality rates was because of different levels of physical activity in different jobs. Since then, many epidemiologic studies have shown that there is a convincing link between physical inactivity and cancers of the colon and breast, and a possible link between physical inactivity and prostate and endometrial cancers. For other cancers, studies have not found a link with physical activity. In this article we will discuss only colon and breast cancers. These are the only cancers for which researchers have found consistent evidence that physical activity can help reduce the risk of cancer.

Table 1:

Genes which can contribute to cancer

TYPE OF GENE	WHAT THE GENE DOES	EXAMPLE OF GENE
Oncogene	Helps cells grow by coding for proteins that stimulate cells to divide or die. When proto-oncogenes mutate, cells can become cancerous.	***Bcl-2,*** a proto-oncogene • altered in many cancers • plays a role in regulating cell death
Tumour Suppressor Gene	Helps limit how often cells divide. When these genes are damaged or missing, cells may divide uncontrollably.	***p53*** • altered in many cancers
Caretaker Gene	Helps keeps genes stable. When these genes are damaged, other genes can mutate.	***BRCA-1,*** the first breast cancer gene identified • contributes to some inherited breast cancers
Gatekeeper Gene	Helps regulate the number of cells. When these genes are damaged, cells divide more rapidly than cells die.	***APC*** • changes in this gene occur early in some forms of colon cancer

Physical activity helps prevent colon cancer

In Canada, colorectal cancer is the second leading cause of cancer death. One of the main risk factors for this cancer is older age; another important risk factor is physical inactivity.

Researchers have carefully investigated how colonic epithelial cells change from normal to malignant. In many people who have non-inherited types of colon cancers, the Kisten-ras (Ki-ras) oncogenes are activated, tumour suppressor genes are lost, and the APC gene mutates or is lost. Exercise may influence genetic changes in colonic epithelial cells, leading to cancer, but there is little empirical research to prove a connection.

More than 100 epidemiologic studies have looked at the link between physical activity and colon cancer. Risk for colon cancer decreases with each hour spent exercising moderately to vigorously. The intensity of physical activity is often expressed as metabolic equivalent task or MET. One MET equals the amount of energy the "average" person expends at rest. One MET is estimated to be 3.5 ml of oxygen per kilogram per minute or 1 kcal per kilogram per hour. Two METs equal twice the amount of energy expended at rest, and so on. The number of MET-hours per week means the METs per hour of each activity multiplied by the number of hours per week that a person engages in that activity (see Ainsworth et al. 2000 for more information). Older adults who did a total of 7 to 13 MET-hours per week of recreational physical activity (walking plus other activities), decreased their risk of colon cancer by 10% compared to people who were not physically active. Older adults who did more than 30 MET-hours per week of physical activity reduced their risk for colon cancer by about 35%.

Physical activity may protect against colon cancer because it speeds the passage of food through the gastrointestinal tract. This reduces how long the body is exposed to potential carcinogens (such as bile acids), to hormones which stimulate cell division (mitogens, including insulin-like growth factors or IGF), and to free radicals that damage DNA. Physical activity also increases immune responses by those cells that can kill tumour cells (at least in lab experiments). However, there is little empirical evidence to show exactly how physical activity helps protect against colon cancer in people.

Physical activity helps prevent breast cancer

Many observational studies have shown that physically active women are less at risk of breast cancer than women who are inactive. So far, no research has used randomized controlled trials to prove that exercise causes the reduced risk. Nevertheless, studies of groups of women have shown that 3 to 4 hours a week of vigorous activity can cut the risk of breast cancer by about 30 to 40%. The risk is reduced even more for postmenopausal women. Women who were physically active as adolescents (at age 12) were less likely to develop breast cancer than women who were less physically active as teenagers.

To date, no studies have linked physical activity with specific changes in oncogenes, tumour suppressor genes, gatekeeper or caretaker genes in breast epithelial cells. Researchers have several theories about how physical activity's effects on the body may help prevent breast cancer. Here are some possible explanations:

- exercise cuts levels of estrogen, which slows cell proliferation,
- exercise increases levels of serum hormone binding globulin (SHBG), which lowers the amount of estrogen available in the body,
- exercise decreases levels of insulin and IGF, thereby reducing signals for cell proliferation and also helping to control body weight,
- exercise enhances the body's natural immunity, so that macrophages and natural killer cells can more easily destroy cancer cells, and
- exercise increases the body's own antioxidant responses, which stifle how much damage free radicals can cause to DNA.

Summary and Recommendations: A healthy lifestyle helps prevent cancer

Accurate measurement of physical activity is often difficult in epidemiological studies and there is limited data on how biological mechanisms help reduce the risk of cancer. However, increased physical activity has overwhelmingly positive effects on health. Individuals who are physically active are more likely to control their body weight and are less likely to be obese. They typically do not smoke, and may be more likely to make healthier dietary choices (such as consuming more fruits and vegetables) than sedentary individuals. Thus, increased physical activity could help prevent cancer directly because of its physiological effects, and indirectly because it is associated with a range of healthy lifestyle factors.

Physical activity during recovery

Common cancer treatments and side effects

Unfortunately, people cannot usually survive cancer without significant medical interventions including major surgery, radiation therapy, and drug treatments such as chemotherapy and hormone therapy. These medical interventions can cause acute and chronic side effects and affect physical functioning and quality of life (QoL). They also increase the risk of second cancers and other major health conditions such as cardiovascular disease, osteoporosis, and obesity. These negative effects are often combined with the declines in health that can occur with aging. How might exercise help older adults offset some of the impact of cancer treatments? Although research has found that exercise is safe and beneficial for cancer survivors in general, very few studies have focused on older adult cancer survivors.

How exercise affects older cancer survivors

The first exercise study to explicitly look at older cancer survivors was undertaken by Demark-Wahnefried and colleagues. They examined the association between self-reported exercise and physical functioning in 688 survivors of breast and prostate cancer between the ages of 60 and 94. After controlling for important demographic and behavioural variables, the researchers found that breast and prostate cancer survivors who did 20 minutes of vigorous exercise at least 3 times a week also scored significantly and meaningfully higher on physical functioning than survivors who did not exercise. The research did not study moderate intensity exercise.

Segal and co-investigators included a substantial number of older cancer survivors in their study of how resistance exercise affected muscular fitness and quality of life (QoL) in prostate cancer survivors being treated with androgen deprivation therapy. More than 70% of the 150 subjects in the study were older than 65. Participants were randomly assigned to different exercise groups for 12 weeks. One group was supervised as they performed nine resistance exercises three times per week at 60 to 70% of their maximum capacity. Members of the control group were not asked to do anything. Results showed that members of the exercise group reported less fatigue and greater QoL than members of the control group. Moreover, the survivors felt that the improvements in fatigue and QoL were large enough to be important. Researchers also discovered that they had become stronger. While the exercise group increased upper-body strength by 41% and lower-body strength by 32%, the control group's strength declined slightly.

In another study of 65 prostate cancer survivors aged 52 to 82, Windsor et al. examined how a home-based, moderate intensity walking program affected fatigue and physical functioning. Participants who were receiving radiation therapy walked three days a week for 30 minutes at 60 to 70% of their maximal heart rate. While the control group found the radiation therapy left them feeling more fatigued, exercise helped prevent fatigue. Moreover, the exercise group's fitness increased significantly while the control group's fitness declined slightly.

These two studies suggest that aerobic and resistance exercise programs can benefit older

prostate cancer survivors, even while they are receiving treatments such as hormone therapy and radiation therapy.

What motivates older cancer survivors to exercise?

Although exercise is likely to benefit older cancer survivors, the disease and treatment may make it hard to motivate older cancer survivors to exercise. Some research shows that older cancer survivors exercise less than their younger counterparts and may exercise for different reasons. For example, whether older cancer survivors feel self-efficacy and perceive that they have control over their own behaviour may be particularly important in determining whether they will exercise. Only one study to date has tried to change exercise behaviour among older cancer survivors. The 6-month randomized controlled trial used a lifestyle intervention for breast and prostate cancer survivors between the ages of 65 and 91. Members of the intervention group received telephone counselling and were given print materials designed to increase exercise and improve diet. Results showed that people in the intervention group ate a significantly improved diet, but did not expend more energy or have improved physical function. This suggests that a low-intensity, distance-based intervention may not be enough to help older cancer survivors increase levels of physical activity.

Summary and Recommendations: Physical activity helps during recovery from cancer

In summary, most Canadians diagnosed with cancer will be older adults that face the double challenge of cancer and aging. There is little information available now about the best kind of exercise program for this underserved group of people, or the best way to reach them. Nevertheless, early research seems to suggest that exercising during and after cancer treatments is safe and can help most older cancer survivors. Even though there are no exercise guidelines specifically for older cancer survivors, health practitioners might consider recommending that they follow Canada's Physical Activity Guide for Older Adults. The American Cancer Society has also recommended that cancer survivors of any age who are otherwise healthy should exercise 30 to 60 minutes a day, at least 5 days each week. Some important precautions for people undergoing cancer treatment are included in the table below, but it is always best to seek advice from your treating physician on how best to care for yourself.

ISSUE	PRECAUTION
Severe Anemia	Delay exercise, other than activities of daily living, until the anemia is improved
Compromised immune function	Avoid public exercise facilities until the white blood cell count returns to safe levels
Severe fatigue	People can stretch for 10 minutes each day if they do not feel able to exercise, and should warm up muscles with gentle activity before stretching
Undergoing radiation	Depending on treatment area, precautions around exposing irradiated skin to chlorine, as in swimming pools, may be necessary
Indwelling catheters	Avoid water or other exposure to microbes. To keep the process in place, avoid resistance training of muscles near the catheter
Significant peripheral neuropathy	For people who are weak or who easily lose their balance, stationary reclining cycling may be better than walking outdoors

Conclusions

Research suggests that physical activity can play an important role in preventing some types of cancer, such as breast and colon cancer. Also, recent research shows that physical activity can help people recover from cancer, during and after treatment. A good way to start preventing cancer and recovering from treatment is to follow *Canada's Physical Activity Guide for Older Adults*.

Funding for this publication was provided by Health Canada and the Public Health Agency of Canada.

The opinions expressed in this publication are those of the authors and do not necessarily reflect the official views of Health Canada and the Public Health Agency of Canada or of ALCOA.

Selected References / Références choisies

Ainsworth, B.E., Haskell, W.L., Whitt, M.C., Irwin, M.L., Swartz, A.M., Strath, S.J., O'Brien, W.L., Bassett, D.R., Jr., Schmitz,, K.H., Emplaincourt, P.O., Jacobs, D.R., Jr., and Leon, A.S. (2000). Compendium of physical activities: An update of activity codes and MET intensities. *Medicine & Science in Sports & Exercise*. 32(9 Supplement): S498-S516.

Canadian Cancer Society. 2006. Canadian Cancer Statistics. Toronto. Available at: *http://www.cancer.ca/vgn/images/portal/cit_86751114/31/21/935505792cw_2006stats_en.pdf.pdf, Table 1*.

Chao, A., Connell, C.J., Jacobs, E.J., McCullough, M.L., Patel, A.V., Calle, E.E., Cokkinides, V.E., and Thun, M.J. (2004). Amount, type, and timing of recreational physical activity in relation to colon and rectal cancer in older adults: the Cancer Prevention Study II nutrition cohort. *Cancer Epidemiology, Biomarkers & Prevention*. 13(12): 2187-2195.

Conn, V.S., Hafdahl, A.R., Porock, D.C., McDaniel, R., and Nielsen, P.J. (2006). A meta-analysis of exercise interventions among people treated for cancer. *Supportive Care in Cancer*. 14(7): 699-712.

Courneya, K.S., Vallance, J.K., McNeely, M.L., Karvinen, K.H., Peddle, C.J., and Mackey, J.R. (2004). Exercise issues in older cancer survivors. *Critical Reviews in Oncology / Hematology*. 51(3): 249-261.

Demark-Wahnefried, W., Clipp, E.C., Morey, M.C., Pieper, C.F., Sloane, R., Clutter Snyder, D., and Cohen, H.J. (2004). Physical function and associations with diet and exercise: results of a cross-sectional survey among elders with breast or prostate cancer. *International Journal of Behavioral Nutrition and Physical Activity*. 1(1): 16.

Demark-Wahnefried, W., Clipp, E.C., Morey, M.C., Pieper, C.F., Sloane, R., Snyder, D.C., and Cohen, H.J. (2006). Lifestyle intervention development study to improve physical function in older adults with cancer: outcomes from project LEAD. *Journal of Clinical Oncology*. 24(21): 3465-3473.

Doyle, C., Kushi, L.H., Byers, T., Courneya, K.S., Demark-Wahnefried, W., Grant, B., McTiernan, A., Rock, C.L., Thompson, C., Gansler, T., Andrews, K.S. for the 2006 Nutrition, Physical Activity and Cancer Survivorship Advisory Committee (2006). Nutrition and physical activity during and after cancer treatment: An American Cancer Society guide for informed choices. *CA: A Cancer Journal for Clinicians*. 56(6): 323-353.

Hanahan, D., and Weinberg, R.A. (2000). The hallmarks of cancer. Cell. 100(1): 57-70. Hoffman-Goetz, L. (2003). Physical activity and cancer prevention: Animal-tumour models. *Medicine & Science in Sports & Exercise*. 35(11): 1828-1833.

Irwin, M.L. (2006). Randomized controlled trials of physical activity and breast cancer prevention. *Exercise and Sport Sciences Reviews*. 34(4): 182-193.

Knols, R., Aaronson, N.K., Uebelhart, D., Fransen, J., and Aufdemkampe, G. (2005). Physical exercise in cancer patients during and after medical treatments: a systematic review of randomized and controlled clinical trials. *Journal of Clinical Oncology*. 23(16): 3830-3842.

Marcus, P.M., Newman, B., Moorman, P.G., Millikan, R.C., Baird, D.D., Qaqish, B., and Sternfeld, B. (1999). Physical activity at age 12 and adult breast cancer risk (United States). *Cancer Causes & Control*. 10(4): 293-302.

Malin, A., Matthews, C.E., Shu, X.-O., Cai, H., Dai, Q., Jin, F., Gao, Y.-T., and Zheng, W. (2005). Energy balance and breast cancer risk. *Cancer Epidemiology, Biomarkers & Prevention*. 15(6): 1496-1501.

McNeely, M.L., Campbell, K.L., Rowe, B.H., Klassen, T.P., Mackey, J.R., and Courneya, K.S. (2006). Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. *Canadian Medical Association Journal*. 175(1): 34-41.

Meyerhardt, J.A., Heseltine, D., Niedzwiechki, D., Hollis, D., Saltz, L.B., Mayer, R.J., Thomas, J., Nelson, H., Whittom, R., Hantel, Al, Schilsky, R.L., and Fuchs, C.S. (2006). Impact of physical activity on cancer recurrence and survival in patients with stage III Colon Cancer: findings from CALGB 89803. *Journal of Clinical Oncology*. 24(22): 3535-3541.

Peters, J., Loud, J., Dimond, E., and Jenkins, J. (2001). Cancer genetics fundamentals. *Cancer Nursing*. 24(6): 446-461.

Quadrilatero, J., and Hoffman-Goetz, L. (2003). Physical activity and colon cancer. A systematic review of potential mechanisms. *The Journal of Sports Medicine and Physical Fitness*. 43(2): 121-138.

Schmitz, K.H., Holtzman, J., Courneya, K.S., Masse, L.C., Duval, S., and Kane, R. (2005). Controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. *Cancer Epidemiology Biomarkers and Prevention*. 14(7): 1588-1595.

Segal, R.J., Reid, R.D., Courneya, K.S., Malone, S.C., Parliament, M.B., Scott, C.G., Venner, P.M., Quinney, H.A., Jones, L.W., D'Angelo, M.E., and Wells, G.A. (2003). Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. *Journal of Clinical Oncology*. 21(9): 1653-1659.

Slattery, M. (2004). Physical activity and colorectal cancer. *Sports Medicine*. 34(4): 239-252.

Slattery, M., Anderson, K., Curtin, K., Ma, K., Schaffer, D., Edwards, S., and Samowitz, W. (2001). Lifestyle factors and Ki-ras mutations in colon cancer tumours. *Mutation Research*. 483(1): 73-81.

Varmus, H., and Weinberg, R.A. (1993). *Genes and the Biology of Cancer*. Scientific American Library, New York, p. 1., ISBN 1040-3213.

Westerlind, K. C. (2003). Physical activity and cancer prevention- Mechanisms. *Medicine & Science in Sports & Exercise*. 35(11): 1834-1840.

Windsor, P.M., Nicol, K.F., and Potter, J. (2004). A randomized, controlled trial of aerobic exercise for treatment-related fatigue in men receiving radical external beam radiotherapy for localized prostate carcinoma. *Cancer*. 101(3): 550-557.