

# **Prescribing Exercise for Cancer Survivors: Time for Physicians to Become More Proactive**

G.A. Watson, G.D. Leonard

Department of Medical Oncology, University Hospital Galway, Galway, Ireland

## **Abstract**

Survivorship has become an integral component of the cancer care continuum. Advances in diagnosis and treatment have resulted in decreasing cancer mortality and a subsequent increase in the cancer survivorship population. International guidelines recommend counselling these patients with regards to healthy lifestyle changes. Increased physical activity has been shown to have profound impacts on quality of life and has also been shown to reduce recurrence rates in patients with breast, colon and prostate cancer. However physicians remain reluctant to prescribe exercise for these patients. Contributing factors include inadequate understanding of the benefits of these programmes, as well as uncertainty with regards to their patients' ability to tolerate such an intervention. It is thus imperative to raise awareness of the benefits of exercise, to guide physicians' selection of patients for exercise and to outline the available options to promote and increase physical activity as part of a healthy lifestyle.

**Keywords:** Cancer survivorship; exercise; colorectal cancer; physical activity; lifestyle

## **Introduction**

Cancer survivorship is a term that may be applied to patients who live with, through and beyond cancer. A cancer survivor may be defined as anyone who has been diagnosed with cancer, from the time of diagnosis through the remainder of his or her life <sup>1</sup>. There has been tremendous progress in the fight against cancer in terms of cancer screening, prevention, early detection and improved treatment strategies. This has resulted in decreased cancer mortality and an exponential rise in the cancer survivorship population. Currently in Ireland there are more than 150,000 cancer survivors <sup>2</sup>. In the US there are over 15 million cancer survivors, and this number is expected to rise to 26 million by 2040 <sup>3</sup>.

Upon completion of systemic cancer treatment, these patients remain at risk of physical deconditioning, nutritional compromise and sarcopenia, or loss of muscle mass, as well as psychosocial sequelae such as depression and anxiety. Thus despite the fact that these patients may be cured of their cancer, the ability to achieve physical, psychological and emotional wellbeing may be a greater challenge. Additional interventions and support such as an exercise programme may be required to achieve this state of wellness, improve quality of life (QOL) and optimise outcomes.

There is ample evidence now that lifestyle changes such as maintaining a healthy weight, increasing physical activity, maintaining a good diet and smoking cessation can reduce cancer recurrence rates, prevent second primary cancers and also prevent long-term sequelae of treatment <sup>3</sup>. Increasing physical activity in particular can result in profound measurable impacts on both physiologic and psychologic wellbeing, and previous studies have demonstrated a positive impact in cardiorespiratory fitness, cancer related fatigue, quality of life and even overall survival <sup>4</sup>. This survival advantage has particularly been reported for breast and colon cancer patients<sup>5,6</sup>.

Unfortunately however there exists a pre-existing paradigm amongst physicians to instead encourage rest for these patients, particularly in patients currently on cancer treatment<sup>3</sup>. One study suggests approximately 20-50% of oncology physicians in Ireland refer their patients for exercise depending on the cancer. This may even be an overestimate due to the challenges and biases in performing such an assessment<sup>7</sup>. This reluctance to refer their patients to exercise programmes is based on a lack of knowledge of the existing data and guidelines, limited instruction with regards to the types of exercise they should be doing and concerns about patient safety and their ability to tolerate such programmes. However international guidelines now clearly recommend counseling these patients with regards to the benefits of physical activity and also encouraging other healthy lifestyle changes. As such it is imperative for treating physicians to be aware of the impact of these changes and these lifestyle modifications must now become a priority for cancer survivors.

### **International Recommendations**

In 2003, the American Cancer Society (ACS) published the first report to provide both healthcare providers and cancer survivors with advice and guidelines pertaining to physical activity in cancer patients. This has since been followed by recommendations from The American College of Sports Medicine (ACSM), the National Comprehensive Cancer Network (NCCN) and the Clinical Oncology Society of Australia (COSA), who all recommend exercise for cancer survivors<sup>8-11</sup>. The general recommendation for patients is to participate in 150 minutes of moderate-intensity aerobic exercise in 3-5 sessions per week and resistance training for major muscle groups on at least 2 days per week as part of a 6-12 week programme<sup>8-12</sup>. Exercise interventions should be provided, at least initially, under supervision by physical therapists or exercise trainers in a health facility or possibly as an unsupervised programme in the home or local gym after initial assessment. Following this home-based unsupervised programmes may be recommended.

### **Physiological Benefits**

Several physiologic changes in the body occur as a result of cancer and its treatment. Chemotherapy can reduce mitochondrial function and impair oxidative phosphorylation in skeletal muscles, resulting in sarcopenia. There may be direct toxic effects, which may impact lung capacity and cardiac reserve<sup>3</sup>. Aerobic exercise however has been shown to combat these effects<sup>13</sup>. Exercise has the potential to affect tumour growth kinetics and metabolism through both physical (eg, increased blood flow, shear stress on the vascular bed, and sympathetic activation) and endocrine (eg, stress hormones and myokines) mechanisms<sup>14</sup>. These effects may also induce increased antitumour immunity by increasing mobilization and infiltration of innate and cytotoxic immune cells in the tumor microenvironment<sup>15</sup>. Moreover, given the close link between tumour metabolism and immunity, physical activity may decrease the production of metabolic byproducts such as lactate, which has been postulated to facilitate tumour growth through its immunosuppressive effects, including impaired activity of natural killer and T cells, disrupted T-cell motility, and increased tumour-permissive activity of tumor associated macrophages<sup>15</sup>.

### **Review Of the Available Evidence**

Approximately 40 large prospective studies have been conducted and confirmed measurable improvements in physical fitness parameters, quality of life (QOL) parameters and in some cases cancer specific outcomes<sup>16</sup>. Multiple systematic reviews of prospective observational studies have demonstrated that physical activity is associated with reduced mortality in breast and colon cancer patients<sup>5,6</sup>. One of the largest prospective observational studies involved 832 patients with stage III colon cancer and examined the effects of self-reported and quantified physical activity at 6 months after completion of chemotherapy. The 3-year disease free survival was 75.1% in patients who exercised for less than 18 metabolic equivalents (MET)-hours (h)/ week as compared with 84.5% in patients who exercised for more than 18 MET-h/week [HR 0.57; 95% CI: 0.39 to 0.85]<sup>5</sup>. Another prospective observational study of 573 women with stages I-III colorectal cancer reported an inverse relationship between the amount of activity post diagnosis and the risk of colorectal cancer-specific and overall survival<sup>17</sup>. Another large and more recent systematic review from exercise studies assessed patients with breast cancer (66%), colorectal cancer (15%) and prostate cancer (14%)<sup>18</sup>. Compared with patients who performed no or less exercise, patients who exercised following a diagnosis of cancer had a lower relative risk of cancer mortality and recurrence. The benefits of increased physical activity has also been reported in patients with recurrent disease and in the metastatic setting<sup>19,20</sup>. Several randomised controlled trials have been performed assessing the impact of physical activity or exercise on quality of

life in patients with colorectal cancer and reported that exercise is safe and feasible in all patients across the disease continuum<sup>20</sup>.

These studies have provided the impetus to initiate large scale randomized phase III trials to definitively assess the efficacy of exercise on cancer survival among cancer survivors. The first randomised controlled trial to investigate the effect of a physical activity intervention on overall and disease-free survival among colon cancer survivors was launched in Canada and Australia in December 2008, the Colon Health and Life-Long Exercise Change (CHALLENGE) trial<sup>21</sup>. CHALLENGE is a 3-year exercise programme involving 962 high risk colon cancer patients (stage II-III) post treatment randomly assigned to structured physical activity over a 3 year period, and results are eagerly awaited. At the University Hospital Galway, in association with Cancer Care West, we have initiated a study evaluating patient's attitudes and compliance towards a recommended exercise intervention. This will hopefully provide additional information with regards to patients' preferences and motivation towards these programmes, ease of access and other potential barriers to participation.

### **Reluctance to Prescribe Exercise**

Despite the plethora of evidence and recommendations, it is estimated that <10% of cancer survivors will be active during treatments and only 20%–30% will be active after treatments<sup>3</sup>. Possible reasons for low adherence rates in this population is the inability to tolerate an exercise programme, lack of enthusiasm or interest, but also lack of awareness of the programmes available.

Medical oncologists have also acknowledged their reluctance to prescribe exercise. Many physicians believe their patients are unable to tolerate such a programme, and this is compounded by the fact that the current infrastructure to provide exercise training for cancer survivors is such that the majority of patients must engage in unsupervised exercise<sup>22</sup>. Oncologists admit to inadequate understanding about the specific dose of exercise necessary to safely improve clinical outcomes, and are unsure how to tailor the recommended exercise guidelines for older patients with multiple comorbidities. Subsequently 84% of oncologists specialising in colorectal cancer in one study did not recommend any exercise to their patients, which may explain why 68% of colorectal cancer survivors are physically inactive after completing curative treatment<sup>23</sup>.

### **Conclusion**

There has been enormous progress in the field of cancer research and the development of precision medicine, where drug therapies are now tailored to individual patients. This personalised approach must now be applied to the survivorship care of our cancer patients. There is emerging evidence that tailored exercise interventions can further optimise patient outcomes. There has been exponential growth in the cancer survivorship population in recent years and this number will continue to grow. There is sufficient evidence that the general population benefit from regular exercise, and we believe this now should be incorporated into the care of cancer survivors, as recommended by international guidelines.

In the future we may well be prescribing exercise for all patients in addition to their standard therapy or surveillance plans. For now however it is imperative that we at least raise awareness and discuss exercise as part of a healthy lifestyle plan particularly for cancer survivors. Such conversations should empower patients, enhance wellness and may even improve survival.

### **Corresponding Author:**

Dr. Gregory Leonard  
Consultant Medical Oncologist  
University Hospital Galway  
Email: Gregory.leonard@hse.ie

### **References:**

1. American Cancer Society: Cancer treatment & survivorship facts & figures 2016-2017.  
<https://www.cancer.org/content/dam/cancer-org/research/cancerfacts-and-statistics/cancer-treatment-and->

- [survivorshipfacts-and-figures/cancer-treatment-and-survivorshipfacts-and-figures-2016-2017.pdf](https://health.gov/health-topics/cancer-treatment-and-survivorshipfacts-and-figures-2016-2017.pdf)
2. <https://health.gov/wp-content/uploads/2017/07/National-Cancer-Strategy-2017-2026.pdf>
  3. Shapiro CL. Cancer Survivorship. *N Engl J Med*. 2018 Dec 20;379(25):2438-2450
  4. Lee K, Tripathy D, Demark-Wahnefried W, Courneya KS, Sami N, Bernstein L, Spicer D, Buchanan TA, Mortimer JE, Dieli-Conwright CM. Effect of Aerobic and Resistance Exercise Intervention on Cardiovascular Disease Risk in Women With Early-Stage Breast Cancer: A Randomized Clinical Trial. *JAMA Oncol*. 2019 Mar 28. doi: 10.1001/jamaoncol.2019.0038. [Epub ahead of print]
  5. Meyerhardt JA, Heseltine D, Niedzwiecki D, Hollis D, Saltz LB, Mayer RJ, Thomas J, Nelson H, Whittom R, Hantel A, Schilsky RL, Fuchs CS. Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803. *J Clin Oncol*. 2006; 24: 3535-3541
  6. Schmid D, Leitzmann MF. Association between physical activity and mortality among breast cancer and colorectal cancer survivors: a systematic review and meta-analysis. *Ann Oncol* 2014;25:1293–1311
  7. Cantwell M, Walsh D, Furlong B, Moyna N, McCaffrey N, Boran L, Smyth S, Woods C. Healthcare professionals' knowledge and practice of physical activity promotion in cancer care: Challenges and solutions. *Eur J Cancer Care (Engl)*. 2018 Mar;27(2):e12795. doi: 10.1111/ecc.12795
  8. NCCN Clinical Practice Guidelines in Oncology: Survivorship. Available from: [https://subscriptions.nccn.org/gl\\_login.aspx?ReturnURL=http://www.nccn.org/professionals/physician\\_gls/pdf/survivorship.pdf](https://subscriptions.nccn.org/gl_login.aspx?ReturnURL=http://www.nccn.org/professionals/physician_gls/pdf/survivorship.pdf)
  9. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvao DA, Pinto BM, Irwin ML, Wolin KY, Segal RJ, Lucia A, Schneider CM, VON Gruenigen VE, Schwartz AL. American college of sports medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc*. 2010; 42(7):1409–1426
  10. Rock CL, Doyle C, Demark-Wahnefried W, Meyerhardt J, Courneya KS, Schwartz AL, Bandera EV, Hamilton KK, Grant B, McCullough M, Byers T, Gansler T. Nutrition and physical activity guidelines for cancer survivors. *CA Cancer J Clin*. 2012
  11. Clinical Oncology Society of Australia. COSA Position Statement on Exercise in Cancer Care. April 2018. <https://www.cosa.org.au/media/332488/cosa-position-statement-v4-web-final.pdf>
  12. Segal R, Zwaal C, Green E, Tomasone JR, Loblaw A, Petrella T. Exercise for people with cancer: a clinical practice guideline. *Curr Oncol*. 2017; 24: 40-46
  13. Alves CR, da Cunha TF, da Paixao NA, Brum PC. Aerobic exercise training as therapy for cardiac and cancer cachexia. *Life Sci*. 2015; 125: 9-14
  14. Hojman P, Gehl J, Christensen JF, Pedersen BK. Molecular Mechanisms Linking Exercise to Cancer Prevention and Treatment. *Cell Metab*. 2018 Jan 9;27(1):10-21
  15. Song M, Chan AT. The Potential Role of Exercise and Nutrition in Harnessing the Immune System to Improve Colorectal Cancer Survival. *Gastroenterology*. 2018 Sep;155(3):596-600. doi: 10.1053/j.gastro.2018.07.038
  16. Jones LW, Alfano CM. Exercise-oncology research: past, present, and future. *Acta Oncol*. 2013; 52: 195-215
  17. Meyerhardt JA, Giovannucci EL, Holmes MD, Chan AT, Chan JA, Colditz GA, Fuchs CS. Physical activity and survival after colorectal cancer diagnosis. *J Clin Oncol*. 2006 Aug 1;24(22):3527-34
  18. Cormie P, Zopf EM, Zhang X, Schmitz KH. The Impact of Exercise on Cancer Mortality, Recurrence, and Treatment-Related Adverse Effects. *Epidemiol Rev*. 2017; 39: 71-92
  19. Jeon J, Sato K, Niedzwiecki D, Ye X, Saltz LB, Mayer RJ, Mowat RB, Whittom R, Hantel A, Benson A, Wigler DS, Atienza D, Messino M, Kindler H, Venook A, Fuchs CS, Meyerhardt JA. Impact of physical activity after cancer diagnosis on survival in patients with recurrent colon cancer: Findings from CALGB 89803/Alliance. *Clin Colorectal Cancer*. 2013 Dec;12(4):233-8. doi: 10.1016/j.clcc.2013.06.005. Epub 2013 Sep 10
  20. Van Blarigan EL, Meyerhardt JA. Role of physical activity and diet after colorectal cancer diagnosis. *J Clin Oncol*. 2015 Jun 1;33(16):1825-34. doi: 10.1200/JCO.2014.59.7799
  21. Courneya KS, Booth CM, Gill S, O'Brien P, Vardy J, Friedenreich CM, Au HJ, Brundage MD, Tu D, Dhillon H, Meyer RM. The Colon Health and Life-Long Exercise Change trial: a randomized trial of the National Cancer Institute of Canada Clinical Trials Group. *Curr Oncol*. 2008 Dec;15(6):279-85
  22. Brown JC, Schmitz KH. The prescription or proscription of exercise in colorectal cancer care. *Med Sci Sports Exerc*. 2014 Dec;46(12):2202-9
  23. Sabatino SA, Coates RJ, Uhler RJ, Pollack LA, Alley LG, Zauderer LJ. Provider counseling about health behaviors among cancer survivors in the United States. *Journal of Clinical Oncology*. 2007; 25(15):2100–2106