

Exercise guidelines for cancer survivors: are fitness and quality-of-life benefits enough to change practice?

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Since the mid-1980s, exercise has been tested as an intervention strategy to help cancer patients prepare for treatments, cope with treatments, and recover after treatments. The field of physical activity and cancer survivorship—"exercise oncology"—began with a trickle of studies published in the mid-1980s that has turned into a torrent of studies published since the first decade of the 2000s. The literature now contains hundreds of studies about the effects of exercise in people who have been diagnosed with cancer (that is, cancer survivors), which have spawned dozens of systematic reviews, several international guidelines, and calls for the integration of exercise programs into clinical and community cancer care.

In this issue of *Current Oncology*, Roanne Segal (a pioneer in the field of exercise oncology) and colleagues report the first Canadian exercise guidelines for cancer survivors¹. The authors followed a rigorous process in developing their guidelines, including appraisal of three existing guidelines, eighteen systematic reviews, and twenty-nine recent randomized controlled trials, and acceptance of comments from independent reviews by several expert panels. The authors correctly conclude that there is sufficient (overwhelming?) evidence that exercise is safe and feasible and that it improves health-related fitness (aerobic fitness, muscular strength) and quality of life for survivors both during and after cancer treatments. Although not explicitly reviewed by the authors, there is also good evidence that exercise improves several cancer-specific symptoms such as fatigue², sleep dysfunction³, and depression⁴.

Based on the evidence, the authors recommend that cancer survivors perform at least 150 minutes of aerobic exercise and 2–3 days of strength exercise weekly—recommendations that are consistent with other general and cancer-specific exercise guidelines. The authors note that their recommendations are intended for policymakers, clinicians, and institutions treating cancer patients in Ontario (and presumably throughout Canada) with the goal of changing clinical practice. The guideline is an important first step in the quest to have exercise programs integrated into cancer care in Canada. However, is evidence of benefit to fitness and quality of life enough to change clinical oncology practice and to make exercise programs an essential component of cancer care?

Certainly, the evidence for fitness and quality-of-life benefits would seem sufficient for clinicians to at least recommend exercise to their patients and perhaps even to refer them to one of the growing number of community-based exercise programs for cancer survivors^{5–9}. But what would it take for cancer centres themselves to integrate high-quality exercise programs into clinical cancer care? The likely answer to that question is evidence of a direct benefit of exercise for cancer outcomes—that is, recurrence, progression, and survival. The authors themselves noted comments from the independent Expert Panel that highlighted the lack of evidence and recommendations with respect to exercise and cancer survival. The authors acknowledged the importance of the question, but lamented the limited quantity and quality of the currently available data.

Fortunately, evidence is rapidly emerging about the potential role of exercise in improving cancer outcomes. A recent systematic review and pooled analysis of twenty-six studies¹⁰ reported that cancer survivors (mostly with breast, colorectal, and prostate cancer) who exercised the most had a 37% lower risk of dying from cancer than did survivors who exercised the least (hazard ratio: 0.63; 95% confidence interval: 0.54 to 0.73). Even more intriguing, there is preliminary evidence that the association between exercise and cancer mortality might vary by specific molecular or genetic markers, suggesting a possible precision medicine approach to exercise oncology. However, as noted by the guideline authors, the evidence to date is based on observational studies. To address that significant limitation, randomized controlled trials are now being conducted to examine the causal effects of exercise on cancer outcomes, and Canada is playing a leading role.

In the first randomized exercise trial to examine long-term cancer outcomes, Courneya *et al.*¹¹ reported an exploratory follow-up of START (Supervised Trial of Aerobic Versus Resistance Training). During 2003–2005, that trial randomized 242 breast cancer patients to usual care ($n = 82$) or to supervised aerobic exercise ($n = 78$) or resistance exercise ($n = 82$) during chemotherapy. After a median follow-up of almost 8 years, disease-free survival was 82.7% in the exercise groups (combined) compared with 75.6% in the control group (hazard ratio: 0.68; 95% confidence interval: 0.37 to 1.24). Although preliminary

and exploratory, START provided the first randomized data to suggest that exercising during breast cancer chemotherapy might actually improve long-term cancer outcomes.

Even more exciting, the first phase III trial designed to examine exercise and cancer outcomes has been launched by our very own Canadian Cancer Trials Group. The CHALLENGE (Colon Health and Life-Long Exercise Change) trial is a multinational phase III investigation of the effects of a 3-year exercise program on disease-free survival in high-risk stage II and III colon cancer patients who have recently completed chemotherapy¹². To date, the trial has demonstrated the feasibility of accrual¹³ and exercise behavior change¹⁴ and has now randomized more than 500 of a planned 962 patients. A second phase III exercise trial has recently been launched by the Movember Foundation with Dr. Fred Saad of the University of Montreal Hospital Centre as one of the study co-chairs. The multinational phase III INTERVAL (Intense Exercise for Survival) trial will examine the effects of a 2-year structured exercise program on overall survival in 866 men with metastatic castration-resistant prostate cancer¹⁵. The foregoing trials, and others like them, will provide the first definitive evidence about the role of exercise in improving cancer outcomes.

Exercise is a low-cost, low-toxicity intervention that improves health-related fitness and quality of life in cancer survivors. If exercise can be shown to improve cancer outcomes, even in a subset of patients, it would likely be adopted by cancer care organizations in Canada and around the world as standard clinical practice. And even if exercise does not improve survival, the message of the first Canadian exercise guidelines for cancer survivors is clear—don't take cancer lying down!

CONFLICT OF INTEREST DISCLOSURES

I have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and I declare that I have none.

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