

Exercise for people with cancer: a clinical practice guideline

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ABSTRACT

Background Development of this guideline was undertaken by the Exercise for People with Cancer Guideline Development Group, a group organized by Cancer Care Ontario's Program in Evidence-Based Care (PEBC). The purpose of the guideline was to provide guidance for clinicians with respect to exercise for patients living with cancer, focusing on the benefits of specific types of exercise, recommendations about screening requirements for new referrals, and safety concerns.

Methods Consistent with the PEBC's standardized approach, a systematic search was conducted for existing guidelines, and systematic literature searches were performed in MEDLINE and EMBASE for both systematic reviews and primary literature. Content and methodology experts performed an internal review, which was followed by an external review by targeted experts and intended users.

Results The search identified three guidelines, eighteen systematic reviews, and twenty-nine randomized controlled trials with relevance to the topic. The present guideline provides recommendations for the duration, frequency, and intensity of exercise appropriate for people living with cancer. It also provides recommendations for pre-exercise assessment, safety concerns, and delivery models.

Conclusions There is sufficient evidence to show that exercise provides benefits in quality of life and muscular and aerobic fitness for people with cancer both during and after treatment, and that it does not cause harm. The present guideline is intended to support the Canadian Society for Exercise Physiology's Canadian physical activity guidelines. The recommendations are intended for clinicians and institutions treating cancer patients in Ontario, and for policymakers and program planners involved in the delivery of exercise programs for cancer patients.

Key Words Exercise, practice guidelines

Curr Oncol. 2017 Feb;24(1):40-46

www.current-oncology.com

INTRODUCTION

Early detection and screening programs and improved medical treatments for certain types of cancer have translated into, or resulted in, more people having a better chance of being cured of their disease or living longer with it. Different tumour types require a variety of treatment interventions depending on prognostic factors such as molecular markers, pathologic subtype, and the extent or stage of the disease. Cancer therapy must therefore be individualized and can include radiation treatment, chemotherapy, hormonal therapy, targeted therapy, or commonly, combinations of those therapies. Consequently, cancer therapy often extends over many months and, in some

cases, years. Although more people are either cured of their disease or receive a more favourable prognostic outcome, those same individuals become physically deconditioned after completion of their therapy¹.

Cancer rehabilitation forms part of the cancer journey. As a result of their cancer or its treatment, many people experience significant physiologic and psychosocial changes that can affect their quality of life (QoL)²—that is, the perceived quality of daily life or an assessment of overall well-being. However, little attention is given to assessing and managing those effects. Exercise has been identified as an intervention to address some of the side effects from treatment and other QoL complications faced by people with cancer². In Ontario, guidelines that provide

evidence-based recommendations on when and how best to implement exercise interventions are needed. Ontario cancer clinicians, exercise consultants, and primary care providers would be able to use such a guideline to provide evidence-based exercise recommendations to their patients. The guideline would also be of interest to Ontario psychosocial oncology administrators who plan programs, including rehabilitation.

Exercise as a prescription is becoming more of a movement throughout the medical field as observed through Exercise Is Medicine Canada (<http://exerciseismedicine.org/canada/>). However, many outcomes of importance with respect to exercise have to be addressed: safety, QOL, and muscular and aerobic fitness, for example. Safety is measured as the occurrence of adverse events as a result of exercise. Quality of life—the perceived quality of a person's daily life, or their ability to enjoy normal life activities and general well-being—has been assessed using various validated scales for cancer patients either undergoing therapy or after completion of treatment. Aerobic capacity or aerobic fitness measures the functional capacity of the cardiorespiratory system. Muscular fitness outcomes include strength measures, commonly upper or lower limb strength. The present guideline's definition of exercise comes from the American College of Sports Medicine: a physical activity causing an increase in energy expenditure and involving a planned or structured movement of the body performed in a systematic manner in terms of frequency, intensity, and duration, and designed to maintain or enhance health-related outcomes³.

There are different types of exercise and exercise programs that can affect QOL and fitness. Aerobic exercise affects the cardiovascular system and depends primarily on oxygen use. Resistance exercise is strength training using weights or elastic resistance bands to overload muscles with the intention of improving strength and endurance⁴. Exercise programs included in this guideline have a definitive aerobic or muscular component, or both. Programs consisting only of behavioural counselling or meditation interventions were excluded.

Exercise programs can have various combinations of aerobic and resistance exercises. For example, the *frequency* or number of times per week a mode or type of exercise is performed could be counted as aerobic exercise 3 times weekly and resistance exercise 2 times weekly. The *duration* of the exercise is the number of minutes of exercise per session. The *intensity* of the exercise refers to the amount of energy expended when performing the activity⁴. Intensity can be measured objectively using heart rate, metabolic equivalents (METS), or the amount of oxygen consumed during an activity. It can also be measured subjectively with a self-reported estimate of effort called the rate of perceived exertion on a scale of 1–10. Low-intensity exercise refers to physical activity or effort performed at 1–3 times the intensity of baseline resting energy expenditure (<3 METS—for example, walking). Moderate-intensity exercise refers to physical activity 3–6 times the intensity of baseline, which requires a moderate amount of effort and noticeably accelerates the heart rate (3–6 METS—for example, brisk walking or cycling). Vigorous-intensity exercise refers to physical activity 6 or more times baseline, which requires a large amount of effort and causes

rapid breathing and a substantial increase in heart rate (>6 METS—for example, running or jumping rope)⁴.

To make clinical practice recommendations, the Working Group of the Exercise for People with Cancer Guideline Development Group synthesized the evidentiary base. Based on the objectives of the guideline, the Working Group derived research questions.

Research Questions

- Does exercise, compared with no prescribed amount of exercise, improve domains of QOL in patients with a diagnosis of cancer?
- Does exercise, compared with no prescribed amount of exercise, improve physical fitness in patients with cancer?
- Does exercise, compared with no prescribed amount of exercise, improve overall survival, disease-specific survival, disease-free survival, or recurrence-free survival in patients with a diagnosis of cancer?
- What is the effect of exercise in terms of safety, adverse events, or injuries for people living with cancer?
- Are results or outcomes different for various intensity levels of aerobic-type compared with resistance-type exercises for people with cancer?
- What delivery models (supervised, unsupervised, combination) are appropriate for patients with different types or stages of cancer?

Target Population

The target population for this guideline consists of adult patients living with cancer, including those on active treatment and those who have completed treatment.

METHODS

The PEBC uses the methods of the practice guidelines development cycle⁵ to produce evidence-based and evidence-informed guidance documents. The process includes a systematic review, quality appraisal and interpretation of the evidence by the Working Group, drafting of recommendations, internal review by content and methodology experts, and external review by Ontario clinicians and other stakeholders.

Step 1: Search for Existing Guidelines and Systematic Reviews

The electronic databases MEDLINE, EMBASE, and Cochrane Database of Systematic Reviews were searched for available literature from January 2005 to October 2013, later updated to January 2014. Using the words “exercise guideline” and “exercise and cancer,” the SAGE (Standards and Guidelines Evidence) Directory of Cancer Guidelines, the U.S. National Guideline Clearinghouse, and the Canadian Medical Association Infobase were searched for existing evidence-based guidelines. A general Internet search using the Google search engine was also conducted to identify additional relevant guidelines. Two Cochrane systematic reviews were identified and form the base of the guideline. Guidelines that were considered relevant to the objectives and the research questions were then evaluated for quality using the AGREE II instrument⁶. Systematic reviews considered relevant were assessed using the AMSTAR tool⁷.

Step 2: Search for Primary Studies

A systematic search for primary studies in MEDLINE (September 2011 through April week 1, 2015) and EMBASE (September week 1, 2011, through April week 2, 2015) used the mesh term “exercise.mp” combined with “neoplasms.mp.” The results were limited to the English language and to randomized controlled trials (RCTs) published from 2011 to 2015. The RCTs were assessed using the Cochrane Risk of Bias tool⁸.

Study Selection Criteria

Articles were considered for inclusion depending on study design and relevance to the research questions. Studies were included if they were RCTs that met these criteria: adult cancer patients and survivors; effects of an exercise regimen compared with usual care; outcomes of QOL and aerobic capacity or muscular fitness; an exercise regimen including repetitive aerobic or resistance exercises; not already included in an identified systematic review; English language (because of unavailability of translation services); and published in 2011 or later.

Synthesizing the Evidence

Because of the clinical heterogeneity of the studies (for example, disease types, treatment status), the nature of the interventions, and the outcomes assessed, a meta-analysis was not possible.

Internal Review

The draft guideline document was circulated to two approval bodies before dissemination to the broader health care community. An Expert Panel comprising medical oncologists, radiation oncologists, physiotherapists, physiologists, medical directors, patient representatives, exercise specialists, and an exercise psychologist contributed to the final interpretation of the evidence and the refinement of the recommendations, and approved the final version of the document. The document was also reviewed by the PEBC Report Approval Panel, whose 3 members have expertise in oncology and guideline methodology.

External Review

The document underwent two external review steps. A targeted peer review was conducted by a small group of invited clinical or methodology experts who reviewed the document and completed a short questionnaire. That group included exercise specialists, professors, researchers, and physiotherapists.

The draft systematic review and practice guideline was also distributed for feedback from health care practitioner groups in the province of Ontario to whom the document was relevant. That group included medical and radiation oncologists, physiotherapists, family practitioners, nurses, and nurse practitioners.

RESULTS

The search for existing guidelines identified eleven publications, of which three were selected for inclusion. The search for systematic reviews identified eighty-four citations, eighteen of which were selected for inclusion. Two

Cochrane systematic reviews were identified and formed the base of the guideline. The search for RCTs yielded 405 citations, 29 of which were included.

Internal Review

Comments from the Expert Panel highlighted the lack of recommendations about exercise and survival. Survival was acknowledged to be an important outcome, but the non-RCT data for survival as an outcome were not robust enough to support the development of recommendations. Other Expert Panel comments were supportive of the recommendations, especially the pre-exercise assessment. The Report Approval Panel comments suggested adding some discussion about the lack of RCT evidence concerning the effect of exercise on survival.

External Review

Five exercise specialists from Ontario considered to be content experts on the topic provided targeted peer review. The guideline was also disseminated to more than 500 Ontario health professionals, 69 of whom provided comments through an online survey. The comments of the reviewers reflected their disappointment with the lack of a more specific exercise regimen for physicians to recommend to their patients and also the lack of information about resources for the patient to be able to exercise. However, reviewers noted that the guideline might prompt clinicians to talk with patients about maintaining a normal active life despite being in treatment or after treatment, and might encourage facilities to dedicate times for those beginning exercise programs.

RECOMMENDATIONS, KEY EVIDENCE, AND INTERPRETATION OF EVIDENCE

Recommendations

1. People living with cancer can safely engage in moderate amounts of exercise (see recommendation 3) while on active treatment or after completion of treatment.
2. Moderate amounts of exercise (see recommendation 3) are recommended to improve the QOL, and muscular and aerobic fitness, of people living with cancer.
3. Clinicians should advise their patients to engage in exercise consistent with the recommendations outlined by the Canadian Society for Exercise Physiology and the American College of Sports Medicine (<http://www.csep.ca/en/guidelines/guidelines-for-other-age-groups>). These are the recommendations for duration, frequency, and intensity:
 - A goal of 150 minutes of moderate-intensity aerobic exercise spread over 3–5 days and resistance training at least 2 days per week is recommended.
 - Resistance sessions should involve major muscle groups 2–3 days per week (8–10 muscle groups, 8–10 repetitions, 2 sets).
 - Each session should include a warm-up and cool-down
4. A pre-exercise assessment to evaluate for any effects of disease, treatments, and comorbidities is recommended for all people living with cancer before they start an exercise intervention.

5. It is recommended that, where possible, people living with cancer exercise in a group or supervised setting, because that environment might provide a superior benefit or outcome in QOL and muscular and aerobic fitness.
6. It is recommended that, where possible, people living with cancer perform exercise at a moderate intensity (3–6 times the baseline resting state) on an ongoing basis as a part of their lifestyle so that improvements in QOL and muscular and aerobic fitness can be maintained for the long term.

Key Evidence

Safety

Two guidelines concluded that exercise is safe for people with cancer both during active treatment and after treatment, and that an assessment evaluating comorbidities and any possible latent effects from treatment that might affect a person's ability to safely engage in exercise and pre-exercise testing are needed to ensure safe exercise conditions^{3,9}. Few adverse events resulting from exercise were reported in the systematic reviews and RCTs. Participants with lymphedema also received QOL benefits, and aerobic and resistance exercises were both considered safe for women who had undergone breast and axillary surgery^{10–14}.

Quality of Life

Fourteen systematic reviews found an improvement in QOL for patients with cancer participating in an exercise intervention during the active treatment or post-treatment period^{11,13,15–28}. Of the sixteen studies involving patients in active treatment^{29–44}, six demonstrated that, compared with the control group, the intervention group experienced significant improvements in QOL^{30,31,33,38–40,43}. In the thirteen post-treatment intervention studies^{10,12,14,45–54}, two reported similar significant differences between groups^{46,49}.

Muscular and Aerobic Fitness

All systematic reviews found positive changes in both muscular and aerobic fitness^{11,13,15–28,55,56}. Of the sixteen RCTs that measured muscular or aerobic fitness, or both^{10,14,29,30,34,35,37,39,40,44–48,52,54}, eleven found significant positive changes in the exercise groups^{10,14,29,30,34,35,37,39,44–46,48}. A systematic review found substantial increases in muscular strength and endurance with resistance training for patients on androgen deprivation therapy²¹.

Pre-exercise Assessment for Evaluation of Effects of Disease Treatments or Comorbidities

The American College of Sports Medicine's Expert Panel developed recommendations for pre-exercise medical assessments to help ensure safety and guide an exercise specialist with respect to an exercise program for a person living with cancer³. One systematic review found that cardiopulmonary exercise testing is a safe, noninvasive method to measure the cardiopulmonary fitness levels of people living with cancer, both during and after treatment²⁷. None of the RCTs reported any adverse events during screening or baseline assessments before initiation of the study intervention^{10,12,14,29–54}.

Exercising in Group or Supervised Setting

Four systematic reviews reported positive results for QOL and muscular and aerobic fitness when the interventions were offered in a group or supervised setting compared with home-based or unsupervised exercise^{15,18,22,55}. Two RCTs compared various settings for interventions and found that the beneficial effects were greater when sessions were supervised, both in groups and by telephone^{39,43}. One RCT found a significant linear trend between an increase in METs performed per week and an improved QOL score for all patients in the study⁵⁴.

Exercising at Moderate Intensity

Three systematic reviews that considered intensity levels and studies of longer length (more weeks) including at least moderate-intensity exercises were associated with improved QOL and muscular and aerobic fitness^{11,18,25}. Another systematic review that evaluated interventions with positive results in QOL found that moderate-intensity aerobic exercise programs were used in the interventions that resulted in a benefit in QOL²⁶. Two RCTs compared different intensity levels of exercise and found improvements in muscular endurance and aerobic capacity for the higher-intensity groups^{40,51}.

Interpretation of the Evidence

Safety, QOL, and Muscular and Aerobic Capacity

Outcomes of importance for the current guideline included safety, QOL, and aerobic and muscular fitness. Numerous studies provide evidence to support an improvement in QOL for patients participating in the interventions. The evidence is of moderate quality. The guidelines scored well on the AGREE II reporting instrument⁵, which evaluates the process of practice guideline development and quality of reporting. The systematic reviews had some issues with heterogeneity in outcomes, populations, and interventions. Issues with the RCTs included active control groups increasing their voluntary exercise volumes, varying adherence rates or no adherence measurements, performance bias, and some questionnaires being targeted to patients in active treatment, which therefore might not be applicable to a post-treatment population.

The published guidelines concluded that exercise is safe for people with cancer. The American College of Sports Medicine³ provides pre-exercise assessment recommendations that include evaluating for peripheral neuropathies, musculoskeletal morbidities, and cardiac issues that might be present as a result of disease, treatment, hormonal manipulation, or metastasis. Exercise is beneficial for enhancing QOL and aerobic and muscular fitness. As with any exercise intervention in an adult population, harm or adverse events can occur, but such events are not negatively influenced by a cancer diagnosis or its therapy; the number of events in the cancer-affected population is similar to the number occurring in the general adult population.

The recommendations allow people living with cancer to determine the mode of exercise (all providing similar benefits) that they would prefer for aerobic and resistance training—for example, running, brisk walking, cycling, weight lifting, or body weight or elastic band exercises.

Pre-exercise Assessment for Evaluation of Effects of Disease, Treatments, or Comorbidities

Undergoing a fitness assessment is a standard recommendation for healthy adults in the general population before they initiate exercise; people living with cancer should therefore also participate in a pre-exercise fitness assessment. The assessment should evaluate comorbidities and any possible latent effects from treatment that might affect a person's ability to safely engage in exercise. Such an assessment would also allow the exercise consultant to modify an exercise program, individualizing it based on the person's physical limitations or vulnerabilities.

It is acknowledged that time and personnel are required for the pre-exercise assessment. However, such assessments can allow clinicians and people living with cancer to feel safer and more secure before an exercise regimen commences. They can also ensure that individuals are aware of possible vulnerabilities associated with their condition.

Exercising in a Group or Supervised Setting

Studies detected a greater and more consistent benefit when the intervention occurred in a group compared with a home (individual) setting. Several systematic reviews assessed the components of successful interventions and concluded that the positive changes in group settings and supervised interventions were substantial.

Almost every intervention started in a supervised setting. A supervised setting can not only provide motivation for an individual to perform exercise, but also potentially allow for an educational component—especially for those performing resistance-type interventions. Safety and exercise options would then both be optimized. Supervision could also allow individuals, who might prefer to exercise outside a group setting, to learn about their options and could ensure that exercise professionals have the opportunity to review and instruct people on how to safely perform or use a specific modality.

Exercising at Moderate Intensity

No study directly compared various intensities or lengths of exercise interventions for people with cancer. The systematic reviews detected a benefit for increasing intensities up to a moderate level (3–6 METs), but greater amounts of exercise did not necessarily further improve outcomes, including QOL. Longer interventions (18 weeks and ongoing) detected a benefit for QOL as well as for aerobic and muscular fitness. Compared with high-intensity exercise, moderate-intensity activity might be sustainable for a longer period of time and could encourage individuals to continue exercise throughout life.

The RCTs were not conducted for a time period adequate for the study of the long-term effects of exercise. Study lengths were associated with the amount of funding and time available to complete the study as opposed to the feasibility or sustainability of an exercise regimen.

IMPLEMENTATION CONSIDERATIONS

The lack of exercise knowledge, funding, facilities, programs, qualified staff, and exercise specialists in cancer

raises concerns. Clinicians or health care professionals might be inexperienced with exercise regimens, and pre-exercise screening for all cancer survivors could be difficult to achieve, given that screening requires additional time and personnel. However, the recommendations presented here will allow patients to choose a preferred activity, and that activity should be promoted as a part of rehabilitative recovery or the survivorship phase of a treatment program.

FUTURE RESEARCH

So far, no studies have been designed to determine more exact exercise programs for specific cancer types. Studies with a longer duration are also needed to determine the long-term effects of exercise, as are studies that compare different intensities to determine the benefits. Evidence that met the inclusion criteria was insufficient to provide recommendations based on survival outcomes.

ACKNOWLEDGMENTS

The authors thank the members of the Exercise for People with Cancer Guideline Development Group for their contributions to the development of this practice guideline. The PEBC is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from the Ontario Ministry of Health and Long-Term Care.

CONFLICT OF INTEREST DISCLOSURES

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

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