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Guideline 19-5

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Exercise for People with Cancer

R. Segal, C. Zwaal, E. Green, J. Tomasone, A. Loblaw, T. Petrella and the Exercise for People with Cancer Guideline Development Group

Report Date: June 30, 2015

Guideline 19-5 is comprised of five sections:

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Guideline 19-5: Section 1

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Exercise for People with Cancer: Recommendations Summary

R. Segal, C. Zwaal, E. Green, J. Tomasone, A. Loblaw, T. Petrella and the Exercise for People with Cancer Guideline Development Group

Report Date: June 30, 2015

GUIDELINE OBJECTIVES

- To provide guidance for clinicians with respect to exercise for patients living with cancer, specifically:
    - Benefits of specific types of exercise
    - Recommendation regarding pre-screening requirements for new referrals
    - Safety concerns

- To provide specific guidance around delivery models and exercise regimens for patients living with cancer at different points in the cancer journey.

TARGET POPULATION

Adult patients living with cancer, including those on active treatment and those who have completed treatment.

INTENDED USERS

Oncologists, exercise consultants, primary care providers, and other members of the healthcare team, such as physiotherapists, kinesiologists, social workers, psychologists, nurses, and occupational therapists.

PREAMBLE

The definition of exercise used in this guideline is any physical activity resulting in an increase in energy expenditure and involving 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 outcomes [1].

There are different types of exercise and exercise programs that can affect quality of life (QoL) and fitness. *Aerobic exercise,* or *endurance training,* impacts the cardiovascular system and depends primarily on oxygen use. *Resistance exercise*, or *strength training,* uses weights or elastic resistance bands to overload the muscle with the intention of improving strength and endurance. The intensity of the exercise dictates the amount of energy that is expended when the exercise is performed. Objective measures of intensity include heart rate, metabolic equivalents (METs), or amount of oxygen consumed during an activity (VO_2). Subjective measures include patient-reported outcomes such as rate of perceived exertion (RPE) on a scale of one to 10. Low-intensity exercise refers to physical activity or effort

performed at one to three times the intensity of baseline resting energy expenditure (<3 METs; e.g., walking); moderate intensity refers to physical activity three to six times the intensity of baseline, which requires a moderate amount of effort and noticeably accelerates the heart rate (3-6 METs; e.g., brisk walking/bike riding); and vigorous intensity refers to physical activity six or more times over baseline, which requires a large amount of effort and causes rapid breathing and a substantial increase in heart rate (>6 METs; e.g., running/jumping rope).

People with cancer who follow the exercise recommendations provided in this document can expect improvements in QoL and aerobic and muscular fitness. The degree of improvement will vary with each person and will be influenced by his or her past and current medical health status. The potential benefits of exercise far exceed the potential associated risks; however, people with cancer should consult with an exercise specialist to understand the modes and amounts of exercise appropriate for them (as per any other adult populations) before starting an exercise program. Cancer-specific modifications to exercise can be found in Appendix 8 [1].

For those who are physically inactive, performing levels of exercise below the recommended levels may bring some benefits. For these adults, it is appropriate to start with small amounts of exercise and gradually increase duration, frequency, and/or intensity under the guidance of an exercise specialist with the goal of meeting the recommendations.

RECOMMENDATIONS

1. People living with cancer can safely engage in moderate amounts of exercise (see Recommendation 3) while on active treatment or post completion of treatment.
2. Moderate amounts of exercise (see Recommendation 3) are recommended to improve the QoL, as well as the 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 of Exercise Physiology and the American College of Sports Medicine. The recommended duration, frequency, and/or intensity are the following:
    - 150 minutes of moderate-intensity aerobic exercise spread over three to five days and resistance training at least two days per week;
    - Resistance sessions should involve major muscle groups two to three days per week (eight to 10 muscle groups, eight to 10 repetitions, two sets); and
    - Each session should include a warm up and cool down.
4. A pre-exercise assessment for all people living with cancer before starting an exercise intervention is recommended to evaluate for any effects of disease, treatments and/or comorbidities.
5. It is recommended, where possible, that people living with cancer exercise in a group or supervised setting as it may provide a superior benefit/outcome in QoL and muscular and aerobic fitness.
6. It is recommended, where possible, that people living with cancer perform exercise at a moderate intensity (three to six 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.

Guideline 19-5: Section 2

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Exercise for People with Cancer: Guideline

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GUIDELINE OBJECTIVES

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- To provide specific guidance around delivery models and exercise regimens for patients living with cancer at different points in the cancer journey.

TARGET POPULATION

Adult patients living with cancer, including those on active treatment and who have completed treatment.

INTENDED USERS

Oncologists, exercise consultants, primary care providers, and other members of the healthcare team, such as physiotherapists, kinesiologists, social workers, psychologists, nurses, and occupational therapists.

PREAMBLE

The definition of exercise used in this guideline is any physical activity resulting in an increase in energy expenditure and involving 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 outcomes [1].

There are different types of exercise and exercise programs that can affect quality of life (QoL) and fitness. *Aerobic exercise,* or *endurance training,* impacts the cardiovascular system and depends primarily on oxygen use. *Resistance exercise,* or *strength training,* uses weights or elastic resistance bands to overload the muscle with the intention of improving strength and endurance. The intensity of the exercise dictates the amount of energy that is expended when the exercise is performed. Objective measures of intensity include heart rate, metabolic equivalents (METs), or amount of oxygen consumed during an activity (VO_2). Subjective measures include patient-reported outcomes such as rate of perceived exertion

(RPE) on a scale of one to 10. Low-intensity exercise refers to physical activity or effort performed at one to three times the intensity of baseline resting energy expenditure (<3 METs; e.g., walking); moderate intensity refers to physical activity three to six times the intensity of baseline, which requires a moderate amount of effort and noticeably accelerates the heart rate (3-6 METs; e.g., brisk walking/bike riding); and vigorous intensity refers to physical activity six or more times over baseline, which requires a large amount of effort and causes rapid breathing and a substantial increase in heart rate (>6 METs; e.g., running/jumping rope).

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For those who are physically inactive, performing levels of exercise below the recommended levels may bring some benefits. For these adults, it is appropriate to start with small amounts of exercise and gradually increase duration, frequency, and/or intensity under the guidance of an exercise specialist with the goal of meeting the recommendations.

RECOMMENDATIONS, KEY EVIDENCE, AND INTERPRETATION

1. **People living with cancer can safely engage in moderate amounts of exercise (see Recommendation 3) while on active treatment or post completion of therapy.**
2. **Moderate amounts of exercise (see Recommendation 3) are recommended to improve the QoL, as well as the 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 of Exercise Physiology and the American College of Sports Medicine. The recommended duration, frequency, and/or intensity are the following:**
    - **150 minutes of moderate-intensity aerobic exercise spread over three to five days and resistance training at least two days per week;**
    - **Resistance sessions should involve major muscle groups two to three days per week (eight to 10 muscle groups, eight to 10 repetitions, two sets); and**
    - **Each session should include a warm up and cool down.**

Key Evidence

Safety

Two guidelines concluded that exercise is safe for people with cancer both during active treatment and post treatment [1,2].

There were very few adverse events due to exercise reported in the systematic reviews and randomized controlled trials (RCTs) (Tables 3 and 4). In particular, those with lymphedema also received QoL benefits, and both aerobic and resistance exercise was safe for women who had undergone breast and axillary surgery [3-7].

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 periods [4,6,8-21] (Table 3).

Of the 16 studies with patients in active treatment [3,22-37], seven had significant differences between the intervention and control groups [22,23,25,30-32,35] (Table 4). In the 13 post treatment intervention studies[3,5,7,38-47], there were three with significant differences found between groups [39,42,43].

Muscular and Aerobic Fitness

All systematic reviews found positive changes in both muscular and aerobic fitness [4,6,8-21,48,49] (Table 3). Of the 15 RCTs that measured muscular and/or aerobic fitness [3,7,22,23,27,28,30,32,37-41,45,47], 11 found significant positive changes in the exercise groups [3,7,22,23,28,30,32,37-39,41] (Table 4). A systematic review found substantial increases in muscular strength and endurance with resistance training for patients on androgen deprivation therapy (ADT) [14] (Table 3).

Interpretation

Outcomes of importance include safety, QoL and aerobic and muscular fitness. Much of the evidence supports an improvement in QoL for those patients participating in the interventions. The evidence is of moderate quality. The guidelines scored well on the AGREE II reporting instrument [51], which evaluates the process of practice guideline development and quality of reporting. The systematic reviews had some issues with heterogeneity due to outcomes, populations, and interventions. RCT issues included active control groups increasing their voluntary exercise volumes, various adherence rates or no adherence measurements, performance bias, and some questionnaires used were targeted at patients in active treatment and, therefore, may not be applicable in a post treatment population.

The published guidelines concluded that exercise was safe for people with cancer.

Exercise is beneficial for enhancing QoL and aerobic and muscular fitness. As with any exercise intervention in an adult population, harm or adverse events may happen, but this is not negatively influenced by the cancer diagnosis or its therapy; it is similar to the number of events in the general adult population.

The recommendations allow for people living with cancer to determine what mode of exercise they would prefer to do for aerobic and resistance training (e.g., running, brisk walking, cycling, weight lifting, body weight or elastic band exercises) with similar benefits.

4. Pre-exercise assessment for all people living with cancer before starting an exercise intervention is recommended to evaluate for any effects of disease, treatments and/or co-morbidities.

Key Evidence

The ACSM guideline Expert Panel developed pre-exercise medical assessments to help ensure safety and to help guide an exercise specialist with respect to an exercise program for a person living with cancer [1] (Appendix 7).

One systematic review found that cardiopulmonary exercise testing (CPET) was a safe, non-invasive method to measure cardiopulmonary fitness levels of people living with cancer, both during and post treatment [20] (Table 3).

None of the RCTs reported any adverse events during pre-screening or baseline assessments before initiation of the study intervention [3,5,7,22-47] (Table 4).

Interpretation

It is a standard recommendation for healthy adults in the general population to undergo a fitness assessment before initiating exercise; therefore, it seems reasonable that people living with cancer should do so as well. The assessment will allow for the evaluation of comorbidities and any possible latent effects from treatment that may affect a person's ability to engage in exercise. As well, it would allow the exercise consultant to modify an exercise program and individualize it for the person with consideration for modifications of standard programs based on physical limitations or vulnerabilities.

It will take time and personnel to perform a pre-exercise assessment. However, it may allow people living with cancer and clinicians to feel safer and more secure before commencing an exercise regimen. It may also ensure these individuals are aware of possible issues regarding their condition.

5. It is recommended, where possible, that people living with cancer exercise in a group or supervised setting as it may provide a superior benefit/outcome in QoL and muscular and aerobic fitness.

Key Evidence

Four systematic reviews found positive results for QoL and muscular and aerobic fitness for exercise when the interventions were offered in a group or supervised setting compared with home-based or unsupervised exercise [11,15,19,48] (Table 3).

Two RCTs compared different settings for interventions and found that the beneficial effects were greater when supervised, both in groups or by phone [32,36]. One RCT

found that for all participants, there was a significant linear trend between an increase in METs performed per week and an improved QoL score [47] (Table 4).

Interpretation

Studies detected a greater and more consistent benefit when the intervention occurred in a group versus a home setting. Several systematic reviews assessed which components were included in 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 may provide motivation for an individual to perform exercise. As well, it may allow for an educational component regarding safety and exercise options for individual people. This may also allow for individuals who might prefer to do exercise outside a group setting to learn about their options and to ensure that exercise professionals have the opportunity to review and instruct people on how to safely perform or use a specific modality.

6. It is recommended, where possible, that people living with cancer perform exercise at a moderate intensity (three to six times 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

There were three systematic reviews that studied intensity levels and found that studies with longer length (more weeks) and those including at least of moderate intensities were associated with improved QoL and muscular and aerobic fitness [4,11,18] (Table 3).

Another systematic review that evaluated interventions with positive results in QoL found that moderate-intensity aerobic exercise programs were used in those interventions that resulted in a benefit in QoL [19] (Table 3).

Two RCTs compared different intensity levels of exercise and found improvements in muscular endurance and aerobic capacity for the higher intensity groups [5,33] (Table 4)

Interpretation

There were no studies that directly compared different intensities or length of exercise interventions with people with cancer.

The systematic reviews detected a benefit for increasing intensities up to a moderate level (6-9 METs), but higher or greater amounts of exercise did not necessarily further improve outcomes including QoL.

As well, longer interventions (18 weeks and ongoing) detected a benefit for QoL as well as aerobic and muscular fitness. Moderate intensities of exercise may also be sustainable for longer periods and may encourage exercise to be continued over a lifetime.

The RCTs were not conducted for an adequate time period to study long-term effects of exercise. In general, study length had more to do with amount of money and time to complete the study as opposed to the feasibility or sustainability of an exercise regimen.

UPDATING

All PEBC documents are maintained and updated through an annual assessment and subsequent review process. This is described in the PEBC Document Assessment and Review Protocol, available on the CCO website at: https://www.cancercare.on.ca/cms/One.aspx?portalId=1377&pageId=122178

FUNDING

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

Information regarding conflict of interest declarations can be found in Appendix 1.

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Guideline 19-5: Section 3

Exercise for People with Cancer: Guideline Methods Overview

The Program in Evidence-Based Care

The Program in Evidence-Based Care (PEBC) is an initiative of the Ontario provincial cancer system, Cancer Care Ontario (CCO). The PEBC mandate is to improve the lives of Ontarians affected by cancer through the development, dissemination, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer control.

The PEBC supports the work of Guideline Development Groups (GDGs) in the development of various PEBC products. The GDGs are composed of clinicians, other healthcare providers and decision makers, methodologists, and community representatives from across the province.

The PEBC is a provincial initiative of CCO supported by the Ontario Ministry of Health and Long-Term Care (OMHLTC). All work produced by the PEBC is editorially independent from the OMHLTC.

Justification for Guideline

As the number of adults surviving a cancer diagnosis and living beyond treatment continues to grow, cancer rehabilitation is becoming an important issue. Many people experience significant physiological as well as psychosocial changes as a result of the cancer or its treatment that can have an impact on morbidity, early mortality, with a notable impact on quality of life (QoL); however, little attention is paid to assessing and managing these effects. Exercise has been identified as an intervention that may address these issues, but guidelines that provide evidence-based recommendations on when and how best to implement exercise interventions in Ontario is needed to move this work forward. Exercise may address the adverse effects from treatment and other QoL issues that are faced by people with cancer.

Guideline Developers

This guideline was developed by the Exercise for People with Cancer GDG (Appendix 1), which was convened at the request of the CCO Psychosocial Oncology Program.

The project was led by a small Working Group of the Exercise for People with Cancer GDG, which was responsible for reviewing the evidence base, drafting the guideline recommendations and responding to comments received during the document review process The Working Group had expertise in medical oncology, radiation oncology, exercise physiology and psychology and health research methodology. Other members of the Exercise for People with Cancer GDG served as the Expert Panel and were responsible for the review and approval of the draft document produced by the Working Group. Conflict of interest declarations for all GDG members are summarized in Appendix 1 and were managed in accordance with the PEBC Conflict of Interest Policy.

Guideline Development Methods

The PEBC produces evidence-based and evidence-informed guidance documents using the methods of the Practice Guidelines Development Cycle [50]. This process includes a systematic review, interpretation of the evidence by the Working Group and draft

recommendations, internal review by content and methodology experts and external review by Ontario clinicians and other stakeholders.

The PEBC uses the AGREE II framework [51] as a methodological strategy for guideline development. AGREE II is a 23-item validated tool that is designed to assess the methodological rigour and transparency of guideline development.

The currency of each document is ensured through periodic review and evaluation of the scientific literature and, where appropriate, the addition of newer literature to the original evidence-base. This is described in the *PEBC Document Assessment and Review Protocol*. PEBC guideline recommendations are based on clinical evidence, and not on feasibility of implementation; however, a list of implementation considerations such as costs, human resources, and unique requirements for special or disadvantaged populations is provided along with the recommendations for information purposes. PEBC guideline development methods are described in more detail in the *PEBC Handbook* and the *PEBC Methods Handbook*.

Search for Existing Guidelines

A search for existing guidelines is generally undertaken prior to searching for existing systematic reviews or primary literature. This is done with the goal of identifying existing guidelines for adaptation or endorsement in order to avoid the duplication of guideline development efforts across jurisdictions. For this project, the following sources were searched for existing guidelines that addressed the research questions:

- Practice guideline databases (Standards and Guidelines Evidence, National Guidelines Clearinghouse, Canadian Medical Association Infobase)
- Guideline developer websites [Scottish Intercollegiate Guidelines Network (UK), National Institute of Clinical Excellence (UK), American Society of Clinical Oncology (USA), National Comprehensive Cancer Network (USA)]

Guidelines that were considered relevant to the objectives and the research questions were then evaluated for quality using the AGREE II instrument [51]. There were no specific selection criteria other than relevance to the guideline objectives.

For this guideline, a search for existing guidelines for adaptation or endorsement yielded an appropriate source document relevant to certain questions. A summary of this process can be found in Section 4. A search of the primary literature was also undertaken for core recommendations (see Section 4: Evidence Review).

Using this evidence, recommendations were drafted and approved by the Exercise for People with Cancer Guideline Development Group.

Guideline Review and Approval

Internal Review

For the guideline document to be approved, 75% of the content experts who comprise the GDG Expert Panel must cast a vote indicating whether they approve the document, or abstain from voting for a specified reason, and of those that vote, 75% must approve the document. In addition, the PEBC Report Approval Panel (RAP), a three-person panel with methodology expertise, must unanimously approve the document. The Expert Panel and RAP members may specify that approval is conditional, and that changes to the document are required. If substantial changes are subsequently made to the recommendations during external review, then the revised draft must be resubmitted for approval by RAP and the GDG Expert Panel.

External Review

Feedback on the approved draft guideline is obtained from content experts and the target users through two processes. Through the Targeted Peer Review, several individuals with content expertise are identified by the GDG and asked to review and provide feedback on the guideline document. Through Professional Consultation, relevant care providers and other potential users of the guideline are contacted and asked to provide feedback on the guideline recommendations through a brief online survey. This consultation is intended to facilitate the dissemination of the final guidance report to Ontario practitioners.

ACKNOWLEDGEMENTS

The Exercise for People with Cancer GDG would like to thank the following individuals for their assistance in developing this report:

- Melissa Brouwers, Sheila McNair, Hans Messersmith, Raymond Poon, Lesley Souter, Donna Maziak, Marko Simunovic, and Kerry Courneya, Lianne Dolan, Kristina Karvinen, Catherine Sabiston and Linda Trinh for providing feedback on draft versions.
- Kristy Yiu and Crystal Su for conducting a data audit.
- Kristine Thornley and Sara Miller for copyediting.

Guideline 19-5: Section 4

Exercise for People with Cancer: Evidence Review

INTRODUCTION

Early detection programs and better medical treatments for certain types of cancer mean that many people have a better chance of surviving the disease or living longer with cancer. Different tumour types require a variety of treatment interventions, depending on prognostic factors such as extent of disease. Therefore, cancer therapy must be individualized and may include radiation treatment, chemotherapy or hormonal therapy, or, commonly, combinations of these 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, these same men and women become physically deconditioned after completion of their therapy.

Cancer rehabilitation forms part of the cancer journey. Many people experience significant physiological as well as psychosocial changes as a result of the cancer or the treatment that can have an impact on quality of life (QoL); that is, the perceived quality of an individual's daily life or an assessment of their well-being. However, little attention is paid to assessing and managing these effects. Exercise has been identified as an intervention to address the side effects from treatment and other QoL issues that are faced by people with cancer.

Guidelines that provide evidence-based recommendations on when and how best to implement exercise interventions in Ontario are needed. Ontario cancer clinicians, exercise consultants, and primary care providers would be able to use this guideline to provide evidence-based exercise recommendations to their patients. It 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 [52].

There are many outcomes of importance with exercise that need to be addressed, such as safety, QoL, and muscular and aerobic fitness. Safety is measured through adverse events occurring as a result of exercise. QoL is an assessment of the perceived quality of a person's daily life or their ability to enjoy normal life activities and general wellbeing. QoL has been assessed using different validated scales for cancer patients either undergoing therapy or after completion of treatment. Aerobic capacity or fitness measures the functional capacity of the cardiorespiratory system. Muscular fitness outcomes included strength measures such as upper or lower limb strength.

The definition of exercise used in this guideline from the American College of Sports Medicine (ACSM) is 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 outcomes [1]. There are different types of exercise and exercise programs that can affect QoL and fitness. Aerobic exercise impacts the cardiovascular system and depends primarily on oxygen use. Resistance exercise is strength training using weights or elastic resistance bands used to overload the muscle with the intention of improving strength and endurance. Exercise programs included in this guideline are ones that had a definitive aerobic or muscular component. Programs with only behavioural counselling or meditation were not included.

Exercise programs can have different combinations of aerobic and resistance exercises. For example, the *frequency* or number of times per week a mode is performed could be aerobic exercises three times a week and resistance exercises two times per week. 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 that is expended when performing that activity. Intensity can be measured objectively using heart rate, metabolic equivalents (METs), or measuring the amount of oxygen consumed during an activity (VO_2) or subjectively with a self-reported estimate of effort called the rate of perceived exertion (RPE) on a scale of one to 10. Low-intensity exercise refers to physical activity or effort performed at one to three times the intensity of baseline resting energy expenditure (<3 METs; e.g., walking); moderate intensity refers to physical activity three to six times the intensity of baseline, which requires a moderate amount of effort and noticeably accelerates the heart rate (3-6 METs; e.g., brisk walking/bike riding); and vigorous intensity refers to physical activity six or more times over baseline, which requires a large amount of effort and causes rapid breathing and a substantial increase in heart rate (>6 METs; e.g., running/jumping rope).

A list of abbreviations can be found in Appendix 2.

To make clinical practice recommendations, the Working Group of the Exercise for People with Cancer Guideline Development Group developed this evidentiary base on which those recommendations are based. Based on the objectives of the guideline, the Working Group derived the research questions outlined subsequently.

RESEARCH QUESTIONS

1. Does exercise improve domains of QoL compared to no prescribed amount of exercise in patients with a diagnosis of cancer?

2. Does exercise improve physical fitness (i.e., strength, VO_2 or aerobic capacity, and objective measures of work done such as distance walked/sit to stand) compared to no prescribed amount of exercise in people with cancer?

3. Does exercise improve overall survival, disease-specific survival, disease-free survival or recurrence-free survival as compared to no prescribed amount of exercise in people with a cancer diagnosis?

4. What is the effect of exercise on people living with cancer in terms of safety, adverse events, or injuries?

5. Are there differential results or outcomes for different intensity levels of aerobic versus resistance types of exercise for people with cancer?

6. What delivery models are appropriate for patients with different types or stages of cancer? Delivery models will be separated into supervised, unsupervised, and combination.

METHODS

This evidentiary base was developed using a planned two-stage method summarized here and described in more detail below.

1. Search and evaluation of existing systematic reviews: If one or more existing systematic reviews are identified that address the research questions and are of

reasonable quality, then those systematic reviews would form the core of the evidentiary base.

2. Systematic review of the primary literature: This review would focus on those areas not covered by existing reviews if any are located and accepted.

Search for Guidelines and Systematic Reviews

Guidelines

The following databases were searched in April 2013 for existing evidence-based practice guidelines that addressed one or more of the preceding clinical questions: the Standards and Guidelines Evidence (SAGE) Directory of Cancer Guidelines, the National Guideline Clearinghouse, and the Canadian Medical Association (CMA) Infobase. In addition, an Internet search using the Google search engine was conducted using the phrases "exercise guideline" and "exercise and cancer" to identify any additional relevant guidelines. Inclusion criteria included adult cancer patients; effects of exercise regimen; outcomes of safety, QoL, aerobic capacity, or muscular fitness; and exercise regimens with repetitive aerobic or resistance exercises. The search was limited to the English language due to the unavailability of translation services. If more than one guideline was identified that addressed a particular research question, then guidelines were selected for further assessment based on currency, clarity, and applicability. Practice guidelines that were selected for further consideration were assessed for reporting quality using the AGREE II [51].

Systematic Reviews

In a scoping search, two Cochrane systematic reviews were identified and it was decided that those systematic reviews would be the base of the guideline. In addition to these systematic reviews, a further search for systematic reviews was conducted. The MEDLINE, EMBASE, and Cochrane Database of Systematic Reviews databases were searched from 2005 to October 2013 and then updated to January 2014 using OVID to identify existing systematic reviews that addressed one or more of the preceding clinical questions. Medical Subject Heading (MeSH) terms related to exercise and cancer were combined with relevant text words and a search filter to identify systematic review citations (see Appendix 3 for the complete search strategy). Inclusion criteria included adult cancer patients; effects of exercise regimen; outcomes of QoL, aerobic capacity, or muscular fitness; and exercise regimens with repetitive aerobic or resistance exercises. The search was limited to the English language due to the unavailability of translation services. If more than one systematic review was identified on the same topic, the most recent review was selected for further assessment. Identified systematic reviews that required further consideration were assessed using the AMSTAR tool [53]. The results of the AMSTAR assessment were used to determine whether an existing review could be incorporated as part of the evidentiary base. Because the two Cochrane systematic reviews were designated as the base of the guideline, it was decided that any other systematic reviews being considered would have to include studies not included in the Cochrane reviews, or be relevant to domains of the guideline other than the ones covered by the Cochrane reviews.

Any identified reviews or evidence-based guidelines that did not meet the preceding criteria, whose AMSTAR or AGREE II assessment indicated important deficiencies in quality, or that were otherwise not incorporated as part of the evidence base are reported in the reference list, but are not further described or discussed.

Primary Literature Systematic Review

Two Cochrane reviews [17,18] were identified that covered all randomized controlled trials (RCTs) until 2011. Therefore, a systematic review of the primary literature was conducted to update those reviews. The following criteria were written to update the literature search from those reviews.

Literature Search Strategy

A systematic search for primary studies was conducted in OVID MEDLINE (September 2011 through April week 1 2015) and OVID EMBASE (week 36 2011 through week 15 2015). The MeSH "exercise.mp or exercise" was combined with "neoplasms.mp" MeSH heading. The results were limited to English language and RCTs published from 2011 to 2015. See Appendix 3 for the full search strategies.

Study Selection Criteria and Protocol

All hits from the OVID literature search were input into reference management software (EndNote X6), where duplicate citations were removed. A review of the titles and abstracts that resulted from the search was performed by one reviewer (CZ). For those items that warranted full-text review, one reviewer (CZ) reviewed each item and consulted the rest of the Working Group whenever there was uncertainty.

Studies were included if they met the following criteria:

- RCTs of the following:
    - Adult cancer patients and survivors
    - Effects of exercise regimen versus usual care
    - Outcomes of QoL and aerobic capacity or muscular fitness
    - Exercise regimen included repetitive aerobic or resistance exercises
    - Not in an included identified systematic review
- English language because of unavailability of translation services
- Published in 2011 or later

Data Extraction and Assessment of Study Quality and Potential for Bias

Data extraction was conducted by one author (CZ) and was reviewed by a second independent individual using a data audit procedure. Disagreements were resolved by consensus. The following data were extracted from each relevant article: author, publication year, study population, number of participants, treatment phase, intervention characteristics, QoL scores, fitness measures, adherence, and adverse events. All extracted data and information were audited by an independent auditor.

The RCTs were assessed using Cochrane's Risk of Bias tool. Judgment of each item includes three categories: low, high, or unclear risk of bias. Items include random sequence generation, allocation concealment, blinding participants, personnel and outcome assessment, incomplete outcome data, selective reporting, and other concerns.

Synthesizing the Evidence

Due to the expected clinical heterogeneity between studies (e.g., disease types, treatment status), the nature of the interventions and the outcomes assessed, meta-analysis was not planned.

RESULTS

Search for Existing Guidelines

The search for existing guidelines identified 11 guidelines of which three [1,2,54] met the inclusion criteria and were retrieved for full-text review. Three guidelines were selected for inclusion and were evaluated using the AGREE II instrument [51] (see Appendix 4 for scores).

Search for Existing Systematic Reviews

The search for existing systematic reviews identified 84 citations, 21 of which were retrieved for full-text review. Two additional reviews were identified through personal contacts. Eighteen reviews [4,6,8-21,48,49] (Table 3) were selected for inclusion and were evaluated for quality using the AMSTAR [53] (see Appendix 5 for scores).

Primary Literature Systematic Review

The search for RCTs yielded 405 citations, 360 of which were retrieved for abstract review and 133 met the inclusion criteria and were retrieved for full-text review (Figure 1). Twenty-nine RCTs [3,5,7,22-47](Table 4) were selected for inclusion and were evaluated using Cochrane's Risk of Bias tool [55] (see Appendix 6 for scores).

Figure 1. Primary Literature Search Results

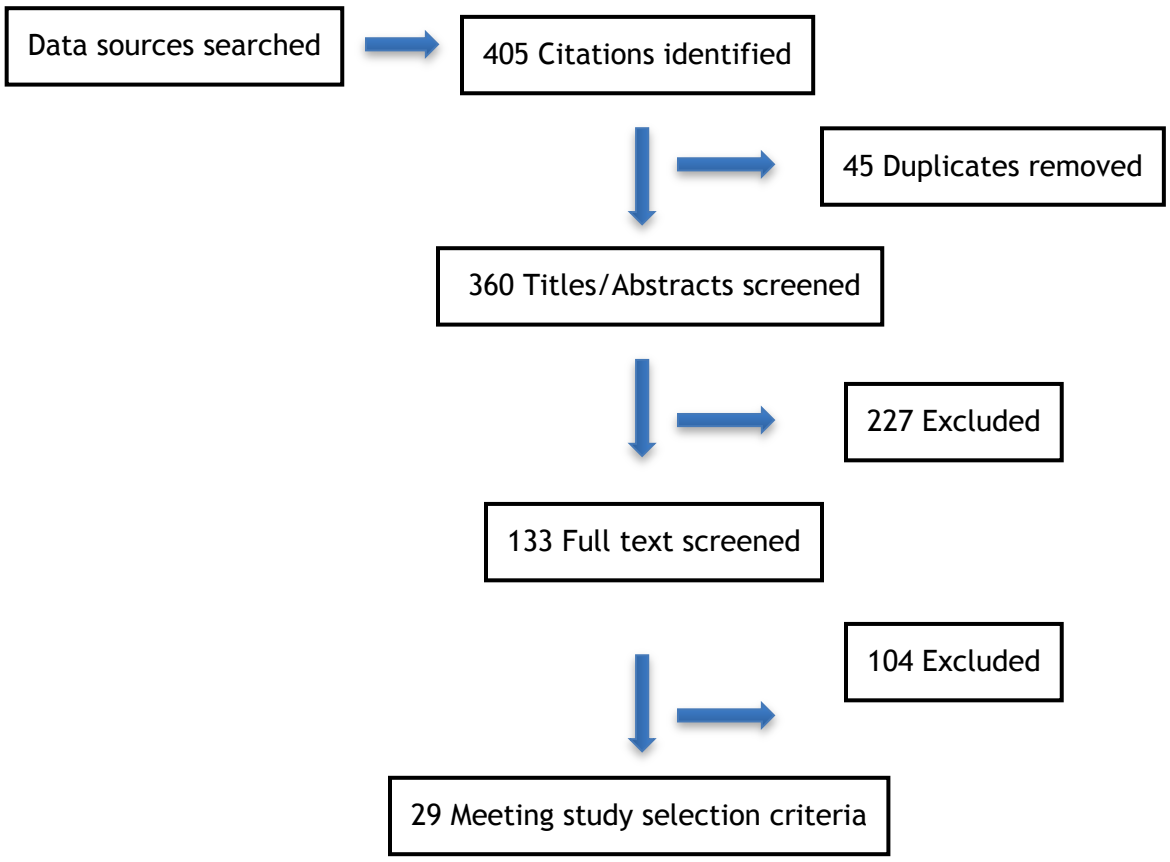

Table 1. Sources selected for inclusion.

Question (exercise compared with usual care)	Number of sources that were included
Does exercise improve domains of QoL?	1 guideline 14 systematic reviews 29 RCTs
Does exercise improve physical fitness (i.e., strength, VO_2 or aerobic capacity, objective measures of work done such as distance walked/sit to stand test)?	1 guideline 8 systematic reviews 18 RCTs
Does exercise improve overall survival, disease-specific survival, disease-free survival or recurrence-free survival?	No systematic reviews of RCTs or RCTs were found
What is the effect of exercise on people with cancer in terms of safety, adverse events or injuries?	2 guidelines 1 systematic review
Are there differential results or outcomes for different intensity levels of aerobic versus resistance types of exercise in people with cancer?	1 guideline 6 systematic reviews 9 RCTs
What delivery models are appropriate for patients with different types or stages of cancer?	1 guideline 2 systematic reviews

Abbreviations: QoL: quality of life; RCT: randomized controlled trial; VO_2: amount of oxygen consumed during an activity

Source Design and Quality

The guidelines were evaluated for reporting quality using the AGREE II [51]. As well, the relevance of the guidelines was evaluated for context and their utility in Ontario recommendations.

The systematic reviews were assessed using the AMSTAR criteria (described at www.AMSTAR.ca). Using these criteria, the scores of the reviews varied, but most scored well. Common limitations were a lack of an a priori design, the lack of the status of publication being used as an inclusion criteria, and a lack of a list of excluded studies. The systematic reviews seemed to focus on different domains of exercise or cancer sites and provided valuable information to inform the questions addressed in this review.

The primary studies included were all RCTs and were evaluated using the Cochrane's Risk of Bias tool [55]. The more common limitations were the lack of: allocation concealment, blinding of participants, personnel and outcome assessment. Other issues included low numbers of participants, no information on pre-intervention exercise levels, the lack of adherence measures to the exercise intervention, and the usual care group increasing exercise levels as much as the exercise group.

Outcomes

The results will be presented in the order of guidelines, systematic reviews, and then RCTs published since the last systematic review. Outcomes of importance include safety, survival, QoL, and aerobic and muscular fitness. Safety is measured using the number of exercise-induced adverse events. QoL has been assessed using different validated scales for cancer patients either in clinical trials or undergoing treatment, such as the European Organisation for Research and Treatment of Cancer (EORTC) QOL-L30, the 36-item Short Form health survey (SF-36), Functional Assessment of Cancer Therapy-Breast (FACT-B), FACT-B for patients with lymphedema (FACT-B+4), Functional Assessment of Cancer Therapy–Prostate (FACT-P) and Patient Oriented Prostate Utility Scale (PORPUS). Aerobic fitness measures the functional capacity of the cardiorespiratory system. Measures of aerobic fitness included the two-, six-, or 12-minute walking test (2MWT, 6MWT, 12MWT), three-minute step test, and maximal or peak oxygen uptake or usage tests (i.e., VO_{2max}, VO_{2peak}). Muscular fitness outcomes included strength measures such as upper or lower limb strength measured in kilograms.

Quality of Life

Guidelines

The Belgian Health Care Knowledge Centre [2], found no conclusive evidence for most cancer types regarding the benefits of exercise treatment.

Systematic Reviews

There have been many systematic reviews examining exercise and cancer patient research to understand whether exercise can improve the QoL of people with cancer. Eighteen systematic reviews were found that studied the effects of exercise on cancer patients [4,6,8-21,48,49](Table 3).

Active treatment

Five systematic reviews conducted a meta-analysis comparing exercise versus usual care on cancer patients during active treatment [4,9,14,18,21](Table 3). A Cochrane review by Mishra et al. [18] summarized the results of studies and found that health-related QoL (HRQoL) improved significantly for both overall QoL change score (the standardized mean difference [SMD] from baseline to 12 weeks) for 12 weeks follow-up (12 groups/11 studies) (HRQoL: SMD=0.47, 95% confidence interval [CI] 0.16 to 0.79 p=0.003; heterogeneity test [I^2]=76%) and overall QoL follow-up values (differences between exercise and control groups' scores) at 12-week follow-up (21 groups/26 studies) (HRQoL: SMD=0.33, 95% CI 0.12 to 0.55 p=0.0024; I^2=68%), and less than six-month follow-up scores (eight groups/six studies) (HRQoL: SMD=0.25, 95% CI 0.07 to 0.43 p=0.0064; I^2=0.0%) for patients with all types of cancer in various exercise regimens. Cavalheri et al. [9] summarized three RCTs studying the effect of exercise on patients following lung resection for non–small cell lung cancer (NSCLC) and did not find a statistical difference (SMD=0.17, 95% CI –0.16 to 0.48 p=0.32; I^2=24%, p=0.27) and Van Haren et al. [21] found three studies with hematological stem cell transplant (HSCT) patients that used in-patient exercise regimens. The QoL weighted mean difference (WMD) was significantly increased for those using the regimen compared with the control group, (WMD=8.72, 95% CI 3.13 to 14.31, p=0.002; I^2=0%, p=0.68). When combining 12 groups from nine studies, Carayol et al. [4] found a significant increase in QoL in patients with breast

cancer due to an exercise intervention (Hedges' g summary effect size=0.343; 95% CI 0.067 to 0.620, p=0.015; I^2=73%; p<0.0001).

Post-treatment

In looking at post-treatment exercise regimens, another Cochrane review by Mishra et al. [17] found that HRQoL improved significantly for both overall QoL change score between baseline and 12-week follow-up (11 studies) (HRQoL: SMD=0.48, 95% CI 0.16 to 0.81, p=0.0032; I^2=78%) and overall QoL follow-up score group differences at 12-week follow-up (16 studies) (HRQoL: SMD=0.49, 95% CI 0.24 to 0.74, p=0.00011; I^2=62%) for patients with all types of cancer in various exercise regimens (Table 3). Ferrer et al. [11] conducted a random effects meta-analysis on 81 post-treatment RCTs and pre-test comparison studies, and found that there was a significant increase in reported QoL using weighted mean effect sizes (*d*+) in patients participating in exercise interventions (*d*+=0.34, 95% CI 0.25 to 0.43; I^2=69%) and that this effect lasted on assessments measured more than six months later (*d*+=0.42, 95% CI 0.23 to 0.61; I^2=76%). The significant increase in QoL was also found by summarizing the effect by using only the RCTs and comparing the exercise group with the control group (*d*+=0.24, 95% CI 0.12 to 0.35; I^2=66%) but not with delayed follow-up of three months (*d*+=0.20, 95% CI -0.058 to 0.46; I^2=36%).

Randomized Controlled Trials

Twenty-nine RCTs were found that studied the effect of exercise on QoL [3,5,7,22-47] (Table 4). Ten used the EORTC QLQ C30 [7,22,24,26,27,37,42,43,46,47], 11 used the SF-36 [5,23,27,28,30,33,35,38-40,44], and nine used a FACT scale [3,25,29,31,32,34,36,41,45]. Twenty-one studies used a combination of aerobic and resistance exercise intervention [3,7,23-25,27-30,32-34,36-40,42,43,46,47], four studies used only resistance training [5,22,31,44] and four used only an aerobic training intervention [26,35,41,45]. The duration of the interventions spanned from six weeks to 12 months. The frequency of exercise sessions ranged from once a week to every day (seven times/week). Sixteen studies were conducted during active treatment [3,22-37] and 13 were after treatment [3,5,7,38-47]. Of the studies with patients on active treatment and compared with usual care, seven had significant differences in QoL between the intervention and control groups [22,23,25,30-32,35]. In the post treatment intervention studies, three studies had a significant difference in QoL between groups [39,42,43].

Muscular Fitness

Systematic Reviews

Strasser et al. [49] conducted a systematic review on resistance training and found increases in upper limb muscle strength ([n=9], WMD=6.90 kg, 95% CI 4.78 to 9.03, p<0.00001; I^2=79%), and lower limb muscle strength ([n=9], WMD=14.57 kg, 95% CI, 6.34 to 22.80, p=0.0005; I^2=91%).

In a review about cancer-related fatigue, McMillan et al. [16] also found a positive effect of exercise interventions on musculoskeletal fitness ([n=5] SMD=0.38, 95% CI 0.18 to 0.59, p>0.001; $X^2_{(4)}$ =8.46, p>0.05).

Using data from three studies, Fong et al. [13] found significant differences in muscular strength between the intervention and control groups for both bench press and leg press (bench press [kg]: SMD=6, 95% CI 4 to 8, p<0.01; I^2=54%, p=0.12; leg press [kg]: SMD=19, 95% CI, 9 to 28, p<0.01; I^2=71%, p=0.03).

Randomized Controlled Trials

Seven studies measured changes in muscle strength using quadriceps leg press to compare differences between the exercise and usual care groups [5,7,22,23,27,37,39]. Six of these found a significant difference between groups in leg strength after the intervention [7,22,23,27,37,39]. Comrie et al. [5] did not find a difference in quadriceps strength but did for chest press and seated row measures.

Aerobic Capacity

Systematic Reviews

McMillan et al. [16] found that exercise interventions had a positive effect on aerobic fitness in a meta-analysis of 12 studies (SMD=0.42, 95% CI 0.32 to 0.51, $p<0.001$; $X^2_{(12)}=20.9$, $p<0.05$ for heterogeneity). Five of the systematic reviews combined studies and found a significant increase in aerobic capacity in the intervention group as compared with the control group measured through VO_{2max}, VO_{2peak}, 6MWD, or treadmill tests [9,10,13,16,48]. Strasser et al. [49], combining two studies, did not find a significant difference in VO_{2max} (WMD=0.97, 95% CI -0.53 to 2.47, p=0.20; $I^2=0$), but did find a significant increase in the 12MWT (WMD=143.65, 95% CI 70.5 to 216.8, p=0.0001; $I^2=0$).

Randomized Controlled Trials

Of the 12 studies that measured aerobic capacity [3,7,23,28,30,32,38-41,45,47], eight found a significant increase in aerobic capacity using VO_{2peak}, 6MWT, a 400 m walk time or a three-minute step test [3,7,23,28,30,32,38,39,41]. Of the three studies that found no significant difference, Saarto et al. [47] did find a significant linear trend between an increase in METs performed per week and an improved QoL score (p=0.01). Both Brocki et al. [40] and Saarto et al. [47] found large increases in physical activity levels in their control groups.

Survival

Exercise and survival is an important issue for people living with cancer. There were no RCTs of people on an exercise intervention versus usual care found that examined survival, disease-free survival or recurrence-free survival in people living with cancer.

Safety

The safety of exercise for adults living with cancer is a very important outcome. These outcomes include measures of adverse events, such as the frequency and type of adverse events during exercise session or whether there was a negative impact on the delivery of the treatment or cancer-specific outcome.

Guidelines

The Belgian Health Care Knowledge Centre [2] developed recommendations concerning the efficacy and safety of exercise treatment during cancer treatment. From the data on the safety of exercise from the systematic literature, no harmful effects of exercise during treatment were found. Thus, it was concluded that exercise is safe for patients undergoing treatment for cancer.

The ACSM [1] convened an expert panel to create a roundtable consensus statement for guidelines about exercise for cancer survivors. They reviewed the literature and concluded that exercise training is safe during and after cancer treatments. They did recommend that specific exercise adaptations could be performed based on disease- and treatment-related adverse effects, such as lymphedema.

Systematic Reviews

In the systematic reviews, eight did not mention any adverse events [4,6,8,9,13,15,19,21], two had no adverse events reported in the studies [10,49] and six of the systematic reviews reported that adverse events were reported in studies in the review [12,14,17,18,48,49].

Randomized Controlled Trials

Sixteen RCTs found no adverse events or side effects due to the exercise program [5,22-24,27,29-33,38,40,42-45]. Eight did not report on adverse events at all [26,28,34,35,37,41,46,47]. Three RCTs reported adverse events that were deemed not related to the intervention [7,25,39] and two reported events due to the intervention [3,36] (three patients had muscle soreness and two had musculoskeletal injury).

Types of Exercise

Resistance Training

Systematic Reviews

Focht et al. [12], analyzing only resistance exercise interventions in both active and post-treatment patients, found that there was a small increase in effect size in QoL (Cohen's *d*=0.25, range -0.72 to 1.14). In one systematic review, Cramer et al. [10] found one study that showed resistance training improved prostate cancer–specific QoL. When looking at both active and post-treatment groups, Strasser et al. [49] found four RCTs comparing resistance training with a non-exercise group that measured QoL. Two of the RCTs detected a significant effect of resistance training on QoL compared with usual care and two detected a trend for improved QoL in the resistance-training group.

Randomized Controlled Trials

Five RCTs used resistance training only for their exercise intervention [5,22,31,42,44]. Winters-Stone et al. [22] and Lonbro et al. [42] both found significant differences in QoL for the exercise group ($p<0.01$ and $p<0.05$ respectively). Rogers et al. [31] found an effect size of d= 0.52 at six weeks and d=0.39 at 12 weeks. Cormie et al. [5,44] did not find significant differences (p=0.195; p=0.475) between groups for QoL (SF-36-mental component summary [MCS]) in both of their RCTs.

Aerobic Training

Systematic Reviews

No systematic reviews investigated RCTs with only an aerobic intervention (no resistance exercise included in the intervention) or RCTs that compared different types of aerobic interventions. Ferrer et al. [11] found aerobic activity intensity was a significant predictor of QoL improvements as a quadratic trend (bivariate moderator analyses ß=0.25, p=0.03).

Randomized Controlled Trials

Pinto et al. [41], Yeo et al. [35], Backman et al. [26] and Broderick et al. [45] used only aerobic interventions in their RCTs. Pinto et al. [41], Backman et al. [26] and Broderick et al. [45] did not find any significant differences between the intervention and control group for QoL, whereas Yeo et al. [35] found a significant difference between the groups on the SF-36-MCS using paired pre-post *t* tests ($p\leq0.05$).

Resistance versus Aerobic Training

Santa Mina et al. [29] compared aerobic and resistance moderate to vigorous-intensity home-based training. No difference was found between the training groups using two measures of QoL; Fact-P (p=0.935) and PORPUS (p=0.625).

Frequency

No systematic reviews or RCTs compared the frequency of the number of sessions of an intervention. The Carayol et al. [4] systematic review evaluated a weekly exercise schedule for patients with breast cancer. Using a regression analysis of 12 studies, they found that an increase in QoL was observed weakly with targeted exercise doses of less than 12 MET hour/week using linear regression (*F*-statistic =9.96, p=0.01; R^2=0.14).

Pastakia et al. [19] conducted a review of RCTs that produced positive results in an effort to determine the parameters of the exercise inventions used with patients with breast cancer. It was found that seven of nine studies used a frequency of three times per week, one had a frequency of two times per week, and one ran the program over the duration of three cycles of chemotherapy.

Mishra et al. [17,18] found that the range of frequency of trials was once per week to daily exercise sessions.

The frequency of exercise sessions in the RCTs ranged from once a week to every day (seven times/week).

Duration of Intervention

The number of weeks that an exercise intervention was conducted was also not directly compared. The Carayol et al. [4] systematic review evaluated the weekly exercise dose of 12 studies (groups) of patients with breast cancer RCTs using regression and found that an increase in QoL was observed with longer duration exercise interventions (≥18 weeks) (*F*-statistic=9.96, p=0.01; R^2=0.14). Ferrer et al. [11] also found, using a model of a weighted least-squares multiple regression, that studies with longer duration (>26 weeks) and greater than 4 METs aerobic exercise increased efficacy significantly (4 METs all intervention groups: Cohen's *d*=0.22, 95% CI. 0.17 to 0.28; high-quality studies: Cohen's *d*=0.16, 95% CI 0.010 to 0.22; 8 METs, all interventions: Cohen's *d*=1.46, 95% CI. 0.90 to 2.03; high quality studies: Cohen's *d*=1.40, 95% CI 0.50 to 2.29).

Mishra et al. [17,18] identified a large variation in the duration of the exercise intervention. The range was from three weeks to one year with the mode being 12 weeks.

The duration of the interventions in the RCTs spanned from six weeks to 12 months.

Intensity

Guidelines

The Canadian Society for Exercise Physiology (CSEP) found that there is a linear dose-response relationship with further health benefits occurring with increased levels of physical activity [54]. Their literature review found that greater health benefits seemed to occur with higher volumes and/or intensities of activity.

Systematic Reviews

Ferrer et al. [11] conducted a bivariate and combined analysis on post-treatment RCTs and pre-test comparison studies and found that lower amounts of aerobic activity (1 MET) were associated with little or no QoL change, but studies of longer duration (26 weeks), and larger volumes of aerobic activity (6-8 METs) were associated with substantial QoL change (Cohen's *d*=1.46, 95% CI 0.90 to 2.03).

Carayol et al. [4] conducted a meta-analysis of exercise interventions using RCTs of patients with breast cancer during treatment. Regression analysis investigating weekly and total exercise dose revealed significant linear models for QoL (linear regression; number of SMD=12, *F*-statistic=9.96, p=0.01; R^2=0.14). An inverse dose-response identified that 12 SMDs magnitude decrease as exercise dose increased (quadratic regression; *F*-statistic=7.13, p=0.02; R^2=0.29).

Mishra et al. [18] concluded that the positive effects of exercise interventions are more pronounced with moderate- or vigorous-intensity versus mild-intensity exercise programs.

Randomized Controlled Trials

Courneya et al. [33] compared women with breast cancer on active treatment in three different exercise levels: 75 minutes of vigorous aerobic exercise per week, 150 minutes of vigorous aerobic exercise per week and 75 minutes of vigorous aerobic exercise per week plus resistance training. There was no significant difference among any of the groups for QoL but they found that higher doses of exercise were achievable and safe.

Comrie et al. [5] compared women with cancer-related lymphedema in three different groups: a high-load resistance exercise group, a low-load resistance exercise group and a usual care group. There was no significant difference among groups for QoL or extent of swelling on the affected arm or severity of symptoms.

Duration of Training Session

No systematic review or RCT compared the number of minutes of a training session. However, in the Mishra et al. [17,18] reviews, the duration of the sessions ranged from 12 to 120 minutes with the mode being 90 minutes (n=13).

Delivery and Facility

Guidelines

The Belgian Health Care Knowledge Centre found no conclusive evidence that allowed for a recommendation in favour of a particular exercise intervention [2].

Systematic Reviews

Pastakia et al. [19] found that all the positive studies in their review were facility-based and under the supervision of a physiotherapist. Ferrer et al. [11] found the intervention efficacy increased when the exercise was supervised (β=−0.26, p<0.01).

Keogh et al. [15] conducted a systematic review for all research designs studying exercise interventions in men with prostate cancer and ranked them into five levels (e.g., a Level 1 study would be an RCT involving >100 participants). These were then graded with the recommendations based on those levels and a summary of the studies. Where Grade A level evidence existed, the benefits of exercise in improving muscular endurance, aerobic endurance, and overall QoL were greatest and appeared greater for group-based exercise rather than home-based, especially if the programs included resistance training.

Jones et al. [48] studies included only trials with supervised training and found a significant benefit in aerobic capacity for all cancer patients together (VO_{2peak}: WMD=2.90, 95% CI 1.16 to 4.64, p=0.001; I^2=87%, p<0.00001) as well patients on active treatment or post-treatment (p=0.0008 and p<0.00001, respectively).

Randomized Controlled Trials

Hayes et al. [32] studied the effect of a face-to-face exercise intervention with a telephone exercise intervention and usual care. For the face-to-face and telephone

interventions, there was clinically meaningful and significant QoL change over time for post-pre scores ($p<0.05$). At the six-month assessment, there was a significant difference for QoL between the telephone intervention group compared with the usual care group ($p \leq 0.05$). Eakin et al. [36] studied the effects of a telephone-based exercise intervention on QoL and found no difference between the intervention and control groups. Brocki et al. [40] compared a group with an exercise program that included one weekly, supervised session plus a home exercise program with a group that only had the home exercise program. They did not find any differences between the two groups $p=0.99$.

Cancer Site-Specific Data

Breast

Systematic Reviews

Two systematic reviews only searched for studies with women with breast cancer [4,6]. Duijts et al. [6] studied the effect of exercise during and post-treatment on QoL. Thirteen studies produced a summary effect size of 0.298 (95% CI 0.12 to 0.48, $p=0.001$). Carayol et al. [4] summarized nine RCTs with 12 intervention groups of patients with breast cancer on active treatment and found that the exercise intervention improved the QoL overall (summary effect size=0.343, 95% CI 0.067 to 0.620, $p=0.015$; $I^2=73\%$, $p=<0.0001$).

Mishra et al. [17,18] conducted a subanalysis using RCTs with patients with breast cancer for different follow-up times and found the effect of the exercise intervention on QoL varied between the time of assessment and whether the participants were in active or post treatment phase.

Randomized Controlled Trials

Seven RCTs studied the effect of an exercise intervention compared with usual care on the QoL of patients with breast cancer [3,5,32,36,43,46,47]. Two were conducted during treatment [32,36] and five were post-treatment studies [3,5,43,46,47]. Only one of the RCTs found a significant difference between the groups [32]. Hayes et al. [32] found a clinically meaningful change over time for the exercise intervention groups and a significant difference between the exercise group with telephone support and the usual care group ($p<0.05$). Saarto et al. [47] found an increase in QoL in both the exercise and the usual care group ($p=0.01$).

Prostate

Systematic Reviews

Gardner et al. [14] evaluated interventions with patients on androgen deprivation therapy (ADT) and found that resistance training substantially and consistently provided increases in muscular strength and that endurance and aerobic training improved muscular strength and endurance to a smaller extent.

Keogh et al. [15] conducted a systematic review for all research designs studying exercise and prostate cancer patients and ranked them into five levels (e.g., a Level 1 study would be an RCT involving >100 participants). These were then graded into recommendations based on levels and a summary of the studies. They found that Grade A level evidence was observed for the benefits of exercise in improving muscular endurance, aerobic endurance, and overall QoL. Grade B evidence also suggested that exercise may improve prostate cancer patients' muscle mass and muscular strength. These effects appeared greater for groups rather than home-based exercise, especially if these programs included resistance training.

Baumann et al. [8] assessed studies comparing exercise interventions in prostate patients both in active and post treatment. It was concluded that supervised exercise is more effective than non-supervised exercise. Recommendations for exercises for prostate patients

included moderate-intensity aerobic training two to three times per week and resistance training two to three times per week to improve muscle strength, aerobic fitness, and QoL.

Mishra et al. [18], in a subanalysis of studies looking at patients on active treatment, found a positive effect of exercise on QoL up to 12 weeks of follow-up (four studies, 242 participants: SMD=0.41, 95% CI 0.15 to 0.67, p=0.0023; I^2=0.0%, p=0.74), but not for more than 12 weeks up to 6 months of follow-up (two studies, 121 participants: SMD=0.28, 95% CI -010 to 0.65, p=0.15; I^2=0.0%, p=0.96).

Focht et al. [12] found four studies that evaluated only prostate cancer patients undergoing ADT and/or radiation therapy. They suggested that resistance exercise is a safe, feasible adjuvant lifestyle intervention approach that results in significant, clinically meaningful improvements in physiologic and QOL outcomes.

Randomized Controlled Trials

Six RCTs evaluated exercise interventions with adults with prostate cancer for QoL [22,23,25,29,39,44]. Five RCTs used people on ADT [22,23,25,29,44] and one comprised of men not on ADT [39]. Five RCTs compared usual care and exercise intervention groups [22,23,25,39,44] and four found significant differences between the groups [22,23,25,39]. Three used a combination of resistance and aerobic interventions [23,25,39] and two used only resistance exercise [22,44].

Non-Small Cell Lung Cancer

Systematic Reviews

For NSCLC, one Cochrane review [9] summarized three small studies and found no significant difference for QoL between the exercise intervention groups and the control groups (SMD=0.17, 95% CI -0.16 to 0.49, p=0.32; I^2=24%, p=0.27).

Randomized Controlled Trials

Stigt et al. [28] asked participants to cycle between a 60 to 80% peak cycling load and added muscle training for three months. They found a significant difference between groups aerobic capacity at three months (p<0.024), but there were also many patients who dropped out of the study. Arbane et al. [27,37] conducted two RCTs with adults with NSCLC comparing usual care with an exercise intervention that occurred on days 1 to 5 after surgery followed by a home intervention. For the home intervention, one study had a four-week home walking program and found a significant difference for participants with airflow obstruction between groups using the SF-36 (p=0.01) [27]. The other RCT added a 12-week exercise program [37]. Neither found a significant difference in QoL after the home interventions for all participants. Brocki et al. [40] used a combination exercise intervention one time per week and found no difference between the usual care and exercise groups for QoL (p=0.99).

Hematopoietic Stem Cell Transplantation

Systematic Review

van Haren et al. [21] summarized three studies measuring changes in QoL after an in-patient exercise regimen. The QoL was significantly increased at the time of discharge for the group receiving the intervention (WMD=8.72, 95% CI 3.13 to 14.31, p=0.002; I^2=0%, p=0.68).

Colorectal

Systematic Reviews

One systematic review analyzed three studies of colorectal cancer patients and found that exercise did not benefit QoL, but did benefit physical fitness. Mishra et al. [17] found a

single study with no significant difference between intervention and control groups (SMD=-0.20, 95% CI. -2.10 to 1.70, p=0.84).

Randomized Controlled Trials

Pinto et al. [41] used a home walking intervention and did not find a significant difference in QoL between usual care and exercise groups.

Head and Neck

Randomized Controlled Trials

Three RCTs, Rogers et al. [31], Lonbro et al. [42] and Samuel et al. [30], found a significant difference in QoL for the exercise intervention compared with the usual care group in people with head and neck cancer ($p<0.05$, $p<0.001$ and $d=0.52$).

Gynecologic

There were not any systematic reviews or RCTs included that focused only on gynecological cancers, exercise, and QoL. The ACSM guideline [1] found only five RCTs with mixed cancer populations that included a small number of gynecological cancer survivors. They believed that the limited data did not allow for recommendations about the safety and/or efficacy of exercise in this population.

Other Cancers

Randomized Controlled Trials

Three RCTs had a combination of cancer sites in the groups. All three did not find a significant difference between usual care and exercise groups for QoL. Oechsle et al. [24] found a significant difference in physical functioning ($p=0.04$) in the exercise group for adults with myeloid leukemia in active treatment but not for overall QoL ($p=0.66$). Porserud et al. [38], when studying an exercise intervention aimed at lower extremities in adults with urinary bladder cancer after a radical cystectomy, did not find a difference in QoL ($p=1.0$) between groups but did find a significant difference in aerobic capacity ($p=0.01$). Yeo et al. [35] found a significant difference in QoL between exercise and usual care groups in adults with pancreatic cancer ($p<0.05$).

Screening Considerations

Guidelines

The ACSM in their expert opinion exercise guideline for cancer survivors developed pre-exercise medical assessments and exercise testing for survivors overall and cancer site-specific medical assessments [1] (See Appendix 7). Their general recommendations include:

- To evaluate for peripheral neuropathies and musculoskeletal morbidities secondary to treatment regardless of time since treatment.
- If there has been a hormonal manipulation, evaluate for fracture risk. This should include consideration for young women who went into early menopause.
- Discern what is safe for individuals with known metastatic disease to the bone.
- Those with known cardiac conditions (secondary to cancer or not) require specific cardiac/medical assessment of the safety of exercise.
- Consult with the patient's medical team to discern the likelihood of metastasis or cardiac toxicity secondary to cancer treatments. This risk will vary widely across the population of survivors.
- For breast cancer, evaluate for arm/shoulder morbidity before upper body exercise.
- For prostate cancer, evaluate for muscle strength and wasting.

- For colon cancer, evaluate for infection prevention behaviours if patient has an existing ostomy before more vigorous exercise training.
- For gynecological cancer, evaluate for lower extremity lymphedema before more vigorous exercise training.
- No exercise testing required before walking, flexibility, and resistance training.
- Follow ACSM guidelines for exercise testing as per outcome of medical assessments.

Systematic Reviews

Steins Bisschop et al. [20] conducted a systematic review to study the feasibility of cardiopulmonary exercise testing (CPET), a non-invasive, objective method of assessing individual cardiopulmonary fitness levels, in cancer patients before an exercise program. They found 28 studies including 1158 patients with different types of cancer. CPET was used successfully for exercise programs before, during, and after cancer treatment. Adverse events occurred in only 1% of patients in whom this screening tool was used. Unfortunately, whether adverse events occurred was described in only 55% of studies. It was thought that the lower VO_{2peak} values of cancer patients compared with healthy persons indicated that exercise should be implemented in a patient's standard care.

Physical Activity Guidelines

The CSEP developed Physical Activity Guidelines for Canadians [54] aimed at children and youth, adults, and older adults. The guidelines for adults are:

- To achieve health benefits, adults aged 18 to 64 years should accumulate at least 150 minutes of moderate- to vigorous-intensity aerobic physical activity per week in bouts of 10 minutes or more.
- It is also beneficial to add muscle and bone strengthening activities using major muscle groups, at least two days per week.
- More physical activity provides greater health benefits.
- Health benefits are described as a reduction in different types of diseases (e.g., premature death, heart disease, stroke, high blood pressure, type 2 diabetes, osteoporosis, overweight, and obesity) and improvement in fitness, strength, and mental health (morale and self-esteem).

The Belgian Health Care Knowledge Centre [2] found no consistent evidence on the benefits of exercise treatment and they were unable to make a recommendation in favour of a particular exercise intervention with the available evidence.

The ACSM found that the benefits to physical functioning and QoL are sufficient to recommend that cancer survivors follow the 2008 Physical Activity Guidelines for Americans with specific exercise programming adaptations [1]. The Key Guidelines for Adults are (see Appendices 7 and 8):

- All adults should avoid inactivity. Some physical activity is better than none, and adults who participate in any amount of physical activity gain some health benefits.
- For substantial health benefits, adults should accumulate at least 150 minutes (2.5 hours) a week of moderate-intensity, or 75 minutes (1.25 hours) a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity. Aerobic activity should be performed in episodes of at least 10 minutes and, preferably, it should be spread throughout the week.
- For additional and more extensive health benefits, adults should increase their aerobic physical activity to 300 minutes (five hours) a week of moderate-intensity, or 150 minutes a week of vigorous-intensity aerobic physical activity, or an equivalent combination of

moderate- and vigorous-intensity activity. Additional health benefits are gained by engaging in physical activity beyond this amount.
- Adults should also do muscle-strengthening activities that are moderate or high intensity and involve all major muscle groups on two or more days per week because these activities provide additional health benefits.

Ongoing Trials

Table 2. Ongoing trials.

Protocol ID	Title and details of trial
NCT02179762	**Vigorous or Moderate Exercise in Enhancing Active Surveillance in Patients With Localized Prostate Cancer.** Randomized 3-arm pilot clinical trial to explore the potential effects of vigorous intensity aerobic exercise (HIIT) using standard cycling and 'cybercycling' compared to moderate intensity standard cycling. Outcomes of interest: QoL, cognition, fitness circulating inflammatory biomarkers and PCa-specific markers of progression (prostate specific antigen [PSA], time to AT) and to explore if these effects may be mediated by changes in body fat.
NCT02050906	**Intensive Diet and Exercise or Standard of Care in Improving Physical Function and Quality of Life in Patients With Prostate Cancer Undergoing Androgen Deprivation Therapy.** This randomized pilot clinical trial studies intensive diet and exercise or standard of care in improving physical function and quality of life in patients with stage IV prostate cancer undergoing androgen deprivation therapy. It is not yet known whether intensive diet and exercise is more effective than standard of care in improving physical function and quality of life in patients with prostate cancer undergoing androgen deprivation therapy. Out comes of interest: functional limitations, body composition, and quality of life.
NCT01140282	**Exercise Program for Early Breast Cancer Survivors.** Inclusion criteria include: Newly diagnosed (I-III) with a first primary invasive breast cancer; have undergone a lumpectomy or mastectomy; have completed neoadjuvant/adjuvant chemotherapy and able to initiate exercise program (if randomized to that arm) within 12 weeks of therapy completion; body mass index (BMI) >25 kg/m^2 or body fat >30% and currently participate in less than 60 minutes of physical activity per week to participate in a 16-week exercise intervention. Out comes of interest include: physical fitness, feasibility of program, reduction in adipose tissue inflammation, improvements in components of metastasis and quality of life.
NCT00639210	**Breast Cancer and Exercise**. A Finnish Breast Cancer Group Study (BREX 01-2004). A multicenter phase III open randomized trial of the efficacy of exercise in the prevention of long-term adverse effects of adjuvant treatments and breast cancer recurrences in women with primary breast cancer. The aim of the study is to investigate whether regular exercise training could reduce the long-term side effects of adjuvant treatments of primary breast cancer and improve quality of life.
NCT00740038	**Support for People Undergoing Chemotherapy.** This study seeks to evaluate the separate and combined effects of stress management training and exercise training on quality of life during chemotherapy treatment. Participants receive either a home-based, self-administered program (stress management, exercise, or stress management + exercise) or usual care (reading materials). It is hypothesized that the combined program (stress management + exercise) will be significantly associated with better quality of life than the usual care group, the exercise only group, and the stress management only group. All participants are assessed at 3 time points: before they begin chemotherapy, 6 weeks after their first chemotherapy infusion, and 12 weeks after their first infusion.
NCT00115713	**Effects of Aerobic Exercise Versus Weight Training in Breast Cancer Survivors During Chemotherapy.** The purpose of this study is to compare the effects of two different types of exercise, aerobic exercise training (AET) and resistance exercise training (RET), on quality of life (QoL) in early stage breast cancer survivors receiving chemotherapy. It is hypothesized that both AET and RET would have beneficial effects on QoL.
NCT00819208	**Health Education Materials With or Without a Physical Activity Program for Patients Who Have Undergone Treatment for High-Risk Stage II or Stage III Colon Cancer.** This randomized phase III trial is studying a physical activity program given together with health

	education materials to see how well it works compared with giving health education materials alone for patients who have undergone treatment for high-risk stage II or stage III colon cancer.
NCT01374399	**Physical Exercise Therapy and Relaxation in Allogeneic Stem Cell Transplantation (PETRA).** The PETRA-Study is a randomized, controlled trial and designed to examine the effects of a one-year physical exercise intervention on side effects, complications and prognosis after allogeneic stem cell transplantation. The exercise intervention includes both resistance and endurance training. Patients assigned to the control group perform a relaxation program (progressive muscle relaxation - Jacobsen) and have the same frequency of social contact.
NCT01515124	**The Women In Steady Exercise Research (WISER) Survivor Trial.** WISER Survivor is a one-year weight loss and exercise study for sedentary breast cancer survivors who are overweight or obese with breast cancer-related lymphedema. There will be four groups: exercise only, weight loss only, exercise and weight-loss combined, and a control group. The purpose of this study is to test the effects of these interventions on lymphedema outcomes, breast cancer recurrence and quality of life.
NCT01106820	**Progressive Resistance Training Versus Relaxation for Breast Cancer Patients During Chemotherapy: Biological Mechanisms and Effects on Fatigue and Quality of Life (BEATE)** The purpose of this randomized intervention study is to investigate the effects and biological mechanisms of a supervised 12-week progressive resistance training on fatigue and quality of life in breast cancer patients during chemotherapy. To determine the effect of the exercise itself beyond potential psychosocial effects due to attention by trainers or the group support, patients in the control group have a comparable training schedule (but with relaxation training.
NCT00929617	**Enhancing Physical Activity Adherence After Breast Cancer Diagnosis (BEAT Cancer II).** Two-arm randomized controlled trial to compare the effects of the 3-month BEAT Cancer physical activity behaviour change intervention to usual care on short and longer-term physical activity adherence among breast cancer survivors. Outcomes of interest: fitness, muscle strength, waist-to-hip ratio, QoL, fatigue, sleep quality and joint dysfunction.

Table 3. Systematic reviews data.

Study	Population, diagnosis	Interventions	Main findings	Comments
Gardner, 2014 [14] *Active treatment*	10 studies; 565 prostate cancer patients with ADT RCTs and pre-post studies	Various exercise interventions	• 5 RCTs and 4 UCTs included QoL measures • 4 studies found significant or clinically meaningful benefits on QoL with exercise training, 5 studies observed no effect • Resistance training consistently provided substantial increases in muscular strength and endurance and smaller improvements with aerobic training	Appropriately prescribed exercise is safe and may ameliorate a range of treatment-induced adverse effects
Cramer, 2014 [10] *Post treatment*	3 studies; 238 colorectal cancer patients	Various exercise interventions	QoL: SMD=0.18, 95% CI -0.39 to 0.76, p=0.53; I^2=59%, p=0.08 Physical fitness: SMD=0.59, 95% CI 0.25 to 0.93, p<0.01; I^2=0%, p=0.44	Adverse events not reported All 3 studies used different treadmill test protocols
Cavalheri, 2013 [9] *Active treatment*	3 studies; 147 patients following lung resection for non-small cell lung cancer	Various exercise interventions	QoL: SMD=0.17, 95% CI -0.16 to 0.49, p=0.32; I^2=24%, p=0.27 The mean range for HRQoL for the control groups was 42.2 to 73.1 and for the intervention groups was 0.17 higher (0.16 lower to 0.49 higher) Exercise capacity: SMD=50.35, 95% CI 15.45 to 85.24, p=0.005; I^2=0%, p=0.59	3 measures of HRQoL: EORTC-C30, SGRQ, SF-36 • 3 different types of exercise • Small number of patients • Different exercise regimens • Assessed at different times
van Haren, 2013 [21] *Active treatment*	3 studies; 148 hematopoietic stem cell transplantation patients	In-patient exercise regimens: some aerobic, some resistance training or structured program. All used EORTC-C30	QoL: WMD=8.72, 95% CI 3.13 to 14.31, p=0.002; I^2=0%, p=0.68	Assessments at discharge
Strasser, 2013 [49] *Active and post treatment*	9 studies; 752 cancer patients	Resistance training	Upper limb muscle strength: WMD=6.90 kg, 95% CI 4.78 to 9.03, p<0.00001; I^2=79%	Resistance training only
	9 studies; 719 cancer patients		Lower limb muscle strength: WMD=14.57 kg, 95% CI 6.34 to 22.80, p=0.0005; I^2=91%	

Study	Population, diagnosis	Interventions	Main findings	Comments
	2 studies; 231 cancer patients		VO_{2max}: WMD=0.97, 95% CI -0.53 to 2.47, p=0.20; I^2=0	
	2 studies; 111 cancer patients		12MWT: WMD=143.65, 95% CI 70.46 to 216.83, p=0.0001; I^2=0	
Focht, 2013 [12] *Active and post treatment*	15 studies; 1077 cancer patients	Resistance exercise	QoL: Cohen's *d*=0.25; range -0.72 to 1.14 Muscular strength: Cohen's *d*=0.86; range 0.11-2.45 Muscular endurance: Cohen's *d*=1.88; range 0.66-2.90	
Carayol, 2013 [4] *Active treatment*	12 groups/9 studies; 1390 breast cancer patients	Various exercise regimens were mixed: aerobic, stretching, resistance training	QoL: Effect size=0.343, 95% CI 0.067 to 0.620, p=0.015; I^2=73%, p=<0.0001 Regression analysis investigating weekly and total exercise dose revealed significant linear models for QoL (linear regression; number of SMD=12, *F*=9.96, p=0.01; R^2=0.14). An inverse dose-response identified that SMD magnitude decreased as exercise dose increased (quadratic regression; number of SMD=12, *F*=7.13, p=0.02; R^2=0.29	Lower to moderate doses of exercise (<12 MET-h/week) consisting in approximately 90–120 min of weekly moderate physical exercise seems more efficacious in improving QoL than higher doses
Steins Bisschop, 2012 [20] *Active and post treatment*	28 studies; 1158 cancer patients	Use of cardiopulmonary exercise testing in cancer patients with continuous gas exchange analysis	CPET was used successfully for exercise programs before, during, and after cancer treatment Adverse events occurred in only 1% of CPET	6 adverse events but only 55% of studies mentioned adverse events
Mishra, 2012 [18] *Active treatment*	12 groups; 806 cancer patients	Various exercise interventions; ≤12-wk follow-up	HRQoL: SMD=0.47, 95% CI 0.16 to 0.79, p=0.003; I^2=76%	Overall quality of life change score
	4 studies; 442 cancer patients	>12-wk follow-up to 6-mo follow-up	HRQoL: SMD=1.25, 95% CI -0.03 to 2.53, p=0.055; I^2=97%	
	4 studies; 282 cancer patients	6-mo follow-up	HRQoL: SMD=0.14; 95% CI -0.11 to 0.39; p=0.26. I^2=0.0%	

Study	Population, diagnosis	Interventions	Main findings	Comments
	21 groups; 1166 cancer patients	≤12-wk follow-up	HRQoL: SMD=0.33, 95% CI 0.12 to 0.55, p=0.0024; I^2=68%	Overall QoL follow-up values
	8 groups; 529 cancer patients	>12-wk follow-up to 6-mo follow-up	HRQoL: SMD=0.25, 95% CI 0.07 to 0.43, p=0.0064; I^2=0.0%	
	8 groups; 686 cancer patients	6-mo follow-up	HRQoL: SMD=0.13, 95% CI -0.09 to 0.35, p=0.25; I^2=45%	
	3 studies; 224 breast cancer patients	≤12-wk follow-up	HRQoL: SMD=-0.37, 95% CI -1.93 to 1.20, p=0.65; I^2=0.0%; p=0.59	
	2 studies; 81 breast cancer patients	6-mo follow-up	HRQoL: SMD=0.24, 95% CI -1.60 to 2.08, p=0.79; I^2=0.0%; p=0.35	
	4 studies; 242 prostate cancer patients	≤12-wk follow-up	HRQoL: SMD=0.41, 95% CI 0.15 to 0.67, p=0.0023; I^2=0.0%; p=0.74	
	2 studies; 121 prostate cancer patients	>12-wk up to 6-mo follow-up	HRQoL: SMD=0.28, 95 % CI -0.10 to 0.65, p=0.15; I^2=0.0%; p=0.96	
Mishra, 2012 [17] *Post treatment*	11 studies; 826 cancer patients	Various exercise interventions; ≤12-wk follow-up	HRQoL: SMD=0.48, 95% CI 0.16 to 0.81, p=0.0032; I^2=78%	Overall QoL change score
	3 studies; 181 cancer patients	>12-wk follow-up to 6-mo follow-up	HRQoL: SMD=0.14, 95% CI 0.38 to 0.66, p=0.61; I^2=64%	
	2 studies; 115 cancer patients	6-mo follow-up	HRQoL: SMD=0.46, 95% CI 0.09 to 0.84, p=0.014; I^2=0.0%	
	16 studies; 760 cancer patients	≤12-wk follow-up	HRQoL: SMD=0.49, 95% CI 0.24 to 0.74, p=0.00011; I^2=62%	Overall QoL values
	5 studies; 353 cancer patients	>12-wk follow-up to 6-mo follow-up	HRQoL: SMD=0.11, 95% CI -0.10 to 0.32, p=0.32; I^2=0.0%	
	2 studies; 115 patients	6-mo follow-up	HRQoL: SMD=0.25, 95% CI -0.12 to 0.62, p=0.18; I^2=0.0%	
	2 studies; 205 breast cancer patients	≤12-wk follow-up	HRQoL: SMD=-0.13, 95% CI -0.41 to 0.14. p=0.34; I^2=0.0%, p=0.36	
	1 study; 52 breast cancer patients	>12-wk up to 6-mo follow-up	HRQoL: SMD=0.99, 95% CI 0.41 to 1.57, p=0.00084	
	2 studies; 110 breast	6-mo follow-up	HRQoL: SMD=0.14, 95% CI -0.24 to 0.51, p=0.47;	

Study	Population, diagnosis	Interventions	Main findings	Comments
	cancer patients		I^2=0.0%, p=0.57	
	1 study; 93 colorectal cancer patients	More than 12-wk up to 6-mo follow-up	HRQoL: SMD=-0.20, 95% CI -2.10 to 1.70, p=0.84	
Keogh, 2012 [15] *Active and post treatment*	12 studies; 498 cancer patients All study designs	Ranked studies into levels 1-5 (RCT >100, RCT <100, etc.) then graded recommendations based on levels and a summary of the studies Studies used EORTC-C30 and SF-36	For overall QoL: • Grade A recommendation for group-based exercise, resistance training • Grade B recommendation for aerobic training For HRQoL: • "B" recommendations for group-based and resistance plus aerobic training • "A" recommendations for group-based exercise for improvements in muscular and aerobic endurance	• Grade A recommendations were given if supported by at least one level 1 study • Grade B recommendations were given when supported by at least one level 2 study Grade C recommendations were given when supported by any non-RCT, level 3-5 studies
Fong, 2012 [13] *Post treatment*	2 studies; 692 patients	Various exercise interventions	QoL (SF-36 mental health): SMD=2.4, 95% CI 0.7 to 4.1, p=0.01; I^2=0%	1 study had 641 patients; other had 51 patients
	5 studies; 147 patients		6MWT: SMD=29, 95% CI 3 to 55, p=0.03; I^2=20%, p=0.288	
	7 studies; 388 patients		VO_{2peak} (mL/kg/min): SMD=2.2, 95% CI 1.0 to 3.4, p<0.01; I^2=18%, p=0.29	
	3 studies; 401 patients		Bench press (kg): SMD=6, 95% CI 4 to 8, p<0.01; I^2=54%, p=0.12 Leg press (kg): SMD=19, 95% CI 9 to 28, p<0.01; I^2=71%, p=0.03	
Baumann, 2012 [8] *Active and post treatment*	21 studies; 2118 prostate cancer patients	Physical activities or exercise interventions	Supervised exercise is more effective than non-supervised exercise Recommends pelvic exercises, aerobic, and resistance training to improve muscular strength, aerobic fitness, and QoL	• Developed recommendations for an exercise program regarding pelvic floor/sphincter training, resistance, or endurance exercise: aims, starting, duration, session length, intensity, etc. Only 7 studies evaluated resistance or aerobic training programs; other pelvic floor/sphincter training

Study	Population, diagnosis	Interventions	Main findings	Comments
Pastakia, 2011 [19] *Active and post treatment*	9 studies; breast cancer patients	Only RCTs with positive results 4 trials used FACT-B measures Implemented between 5 wk to 6 mo	Summarized the interventions used Mode: all trials included a warm up and cool down with an element of flexibility in the program • 4 used only aerobic • 1 used repeated limb movements with a chair • 2 used a combination of aerobic and strengthening • 1 used only strength • All that used strengthening focused on low weights and high reps Duration: range 14-60 min • 4 used 60-min session • 4 progressed from 14-35 min • 1 did not report Frequency: • 7: 3×/week • 1: 2×/week • 1: 3×/week during 3 cycles of CT Intensity: • Aerobic: 4 used 25%-85% HR_{max}, 1 trial used 60%-70% of 1 repetition maximum, 2 trials used 50%-80% VO_{2max}, 1 used moderate level Delivery and location: all programs were gym-based and under supervision of physiotherapist	Developed recommendations for an exercise program
McMillan, 2011 [16] *Active and post treatment*	15 studies; 1061 cancer patients	Various exercise interventions	Aerobic fitness: SMD=0.42, 95% CI 0.32 to 0.51, p<0.001; $X^2_{(12)}$=20.9, p<0.05	Most studies had moderate-intensity aerobic or resistance exercise
	5 studies; 419 cancer patients		Musculoskeletal fitness: SMD=0.38, 95% CI 0.18 to 0.59, p>0.001; $X^2_{(4)}$ =8.46, p>0.05	
Jones, 2011 [48] *Active and post treatment*	6 studies; 571 cancer patients	Various exercise interventions	VO_{2peak}: WMD=2.90, 95% CI 1.16 to 4.64, p=0.001; I^2=87%, p<0.00001	Looked at effects of supervised training on VO_{2peak}
	3 studies; 86 cancer patients	After treatment	VO_{2peak}: WMD=3.36, 95% CI 2.20 to 4.53, p<0.00001; I^2=0%, p=0.93	
	2 studies; 363 cancer patients	During treatment	VO_{2peak}: WMD=1.21, 95% CI 0.50 to 1.92, p=0.0008;	

Study	Population, diagnosis	Interventions	Main findings	Comments
			I^2=0%, p=0.48	
Duijts, 2011 [6] *Post treatment*	12 studies; 1699 breast cancer patients	Various exercise interventions	HRQoL: ES=0.298, 95% CI 0.12 to 0.48, p<0.001; Cochran's Q (p=0.001); Publication bias (p=0.034)	Regression detected heterogeneity for HRQoL due to follow-up time and whether the intervention consisted of individual or group sessions
Ferrer, 2011 [11] *Post treatment*	81 studies; cancer patients	Various exercise interventions	QoL: all studies immediate follow-up WMD=0.34; 95% CI 0.25 to 0.43; I^2=69% Weighted least-squares multiple regression, >26 weeks intervention + 4 METs All intervention groups: Cohen's *d*=0.22, 95% CI 0.17 to 0.28 High-quality studies: Cohen's *d*= 0.16, 95% CI 0.010 to 0.22 >26 week intervention +8 METs All interventions groups: Cohen's *d*=1.46, 95% CI 0.90 to 2.03 High-quality studies: Cohen's *d*=1.40, 95% CI 0.50 to 2.29 Intervention efficacy increased when the exercise was supervised (ß=−0.26, p <0.01)	• Included RCTs and pre-test comparison • Evaluated study length and increase in aerobic METs
	21 studies; cancer patients		QoL: Delayed follow-up (3 mos) WMD=0.42, 95% CI 0.23 to 0.61; I^2=76%	
	53 studies; cancer patients		QoL: RCTS only: immediate follow-up WMD=0.24, 95% CI 0.12 to 0.35; I^2=66%	
	10 studies; cancer patients		QoL: RCTS only: Delayed follow-up WMD =0.20, 95% CI -0.058 to 0.46; I^2=36%	

Abbreviations: ADT: androgen deprivation therapy; CI: confidence interval; EORTC C-30: European Organization for Research and Treatment of Cancer; FACT-B: Functional Assessment of Cancer Therapy – Breast; HRQoL: health-related quality of life; mo: month; MWT: minute walking test; pt: patient; RCT: randomized controlled trial; RT: resistance training exercise; QoL: quality of life; SF-36: Short Form (36) Health Survey; SGRQ: St. George Respiratory Questionnaire; SMD: standardized mean difference; UCT: uncontrolled trial; VO_2: volume of oxygen; wk: week; WMD: weighed mean difference.

Table 4. Randomized controlled trials data.

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
Winters-Stone, 2015 [22] *Active treatment*	29 exercise intervention; 22 control group	Adults with prostate cancer undergoing ADT	Two supervised resistance training sessions with free weights and one home-based resistance band session per week. Control group did stretching exercises.	3x/wk for 12 mo	No study-related injuries occurred.	**QoL (EORTC QLQ C30 –physical function)** score at baseline, 6 and 12 mo Exercise: 87.5 (SD=14.3); 92.2 (SD=11.7); 93.3 (SD=9.0) Control: 89.7 (SD=15.3); 82.4 (SD=20.1); 86.7 (SD=20.7) Difference between groups at 6 mo: p<0.01 Difference between groups at 12 mo: p<0.01 **Quadriceps strength (leg press 1RM, kg)** score at baseline, 6 and 12 mo Exercise: 121.3 (SD=33.5); 137.5 (SD=44.3); 142.4 (SD=52.2) Control: 119.9 (SD=30.3); 121.8 (SD=33.4); 120.8 (SD=30.6) Difference between groups at 6 mo: p=0.03 Difference between groups at 12 mo: p=0.01	• Retention in the study was 84%, (90% in the exercise group and 75% in the control group) • Median attendance to supervised classes was 84% in the resistance group.
Cormie, 2015 [23] *Active treatment*	32 exercise intervention; 31 usual care	Adults with prostate cancer undergoing ADT	Supervised group sessions involving moderate-high intensity aerobic (70-85% maximum heart rate) and resistance exercises of major muscle groups. Sessions were progressive and participants were encouraged to supplement with home-based moderate intensity aerobic exercise for at least 150 min.	1 hr 2x/wk for 3 mo plus home-based 150 min/wk	No adverse events occurred.	**QoL (SF-36 MCS)** score at baseline and 3 mo Exercise: 54.1 (SD=7.9); 56.0 (SD=6.3) Usual care: 53.1 (SD=10.0); 51.8 (SD=9.6) Difference between groups: p=0.022 **Aerobic capacity (VO_{2peak}, mL/kg/min)** at baseline and 3 mo Exercise: 22.1 (SD=3.5); 22.7 (SD=3.8) Usual care: 23.2 (SD=3.4); 22.7 (SD=3.6) Difference between groups:	

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
			The usual care group was offered the program after the study was completed.			p=0.004 **Quadriceps strength (leg press 1RM, kg)** score at baseline and 3 mo Exercise: 134.3 (SD=50.0); 157.9 (SD=52.9) Usual care: 143.6 (SD=52.4); 141.7 (SD=9.6) Difference between groups: p<0.001	
Porserud, 2014 [38] *Post treatment*	9 exercise intervention; 9 usual care	Adults with urinary bladder cancer after radical cystectomy	Supervised group strength and endurance training for lower extremities such as walking and strengthening exercises, balance, mobility and stretching exercises. They were also instructed to take self-paced walks for at least 15 minutes 3 to 5 days a week. The usual care group was offered the program after the study was completed.	45 minutes 2x/wk for 12 wks plus 15 minute walks 3 to 5 times per wk	No adverse events due to the intervention were reported.	**QoL (SF-36 mental health score)** Increase from baseline to 12 wks and 12 wks to 1 year Exercise: 5.6 (SD=10.0); 2.4 (SD=5.6) Usual care: 2.1 (SD=16.0); 0.4 (8.1) Difference between groups after training: p=1.00 Difference between groups at 1 year: p=0.67 **Aerobic capacity (6MWT)** Increase from baseline to 12 wks and 12 wks to 1 year Exercise: 112.9 (SD=40.1); 23.8 (SD=8.2) Usual care: 62.8 (SD=26.3); -19.2 (SD=15.3) Difference between groups after training: p=0.013 Difference between groups at 1 year: p=0.010	• Small sample size • Many dropouts • Exercise group attended 76% (SD=67-95) of group exercise sessions and took daily walks 87% (SD=56-100) of the days

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
Oechsle, 2014 [24] *Active treatment*	24 exercise intervention; 24 usual care	Adults with acute myeloid leukemia undergoing myeloablative chemotherapy and high-dose chemotherapy	Individually supervised with ergometer training for 10-20 minutes and strength exercises for major muscle groups 20 minutes 5 times per week while in hospital. Control group received no specific physical training but were allowed to undergo physiotherapy as medically indicated.	5x/wk for hospital duration Median duration was 21 days (range 16-33 days)	No adverse events were found.	**QoL (EORTC-QLQ-C30)** Overall score for physical functioning Exercise: 50 Usual care: 50 Between-group differences: p=0.66	• No comparison for muscle strength • Small sample size • Significant difference for physical Function al QoL
Galvao, 2014 [39] *Post treatment*	50 exercise intervention; 50 control group	Adults with prostate cancer who had previously been treated with ADT and radiation (>5yr)	Combined supervised progressive group resistance training of major muscle groups and 20-30 min cardiovascular exercises at 70-85% maximum heart rate. Plus two aerobic exercise sessions at home each week. Control group received printed materials about physical activity and a pedometer.	4x/wk for 6 mo; then home-based sessions for mo 7-12	One participant with preexisting back pain, and one with preexisting knee injury withdrew from exercising; one died from lung cancer and one had a nonfatal myocardial infarction.	**QoL (SF-36 v2 MCS)** at baseline, 6 mo and 12 mo scores Exercise: 50.3 (SD=9.6); 51.6 (SD=6.6); 51.2 (SD= 7.5) Control: 47.4 (SD=10.4); 47.1 (SD=9.5); 48.7 (SD=9.5) Between-group difference at 6 mo: p=0.025 Between-group difference at 12 mo: p=0.649 **Aerobic capacity** (400 m walk time in seconds) at baseline, 6 mo and 12 mo Exercise: 288.0 (SD=7.6); 269.4 (SD=8.4); 270.4 (SD= 7.3) Control: 276.5 (SD=7.6); 279.4 (SD=8.4); 274.1 (SD=7.3) Between-group difference at 6 mo: p=0.029 Between-group difference at 12 mo: p=0.028 **Quadriceps strength** (leg extension in kg) at baseline, 6 mo and 12 mo Exercise: 50.7 (SD=3.0); 59.3	• Physical activity recommendations given to the control group (should do over 150 minutes of moderate activity per week)

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
						(SD=3.0); 56.6 (SD=2.8) Control: 51.0 (SD=2.9); 49.9 (SD=2.9); 50.2 (SD=2.8) Between group difference at 6 mo: p<0.001 Between group difference at 12 mo: p=0.011	
Brocki, 2014 [40] *Post treatment*	41 exercise intervention; 37 control group	Adults with surgical resected lung cancer	Supervised, group-based exercise training sessions. Included aerobic exercises with target intensity of 60% to 80% of work capacity and resistance training. Both groups were given home exercise instructions and training diaries.	1 hour 1x/wk for 10 wks	No adverse events were found.	**QoL (SF-36 v2 MCS)** at baseline, 4 mo change and 1 year change score Exercise: 45.67; 4.4; 5.33 Control: 44.88; 5.4; 9.6 Between-group difference at 4 mo: p=0.99 Between-group difference at 1 year: p=0.27 **Aerobic capacity (6MWT)** at baseline, 4 mo change and 1 year change score Exercise: 427m; 61m; 65 m Control: 407m; 55m; 60m Between-group difference at 4 mo: p=0.57 Between-group difference at 1 year: p=0.93	• 43% the control group regularly exercised at home or joined an exercise program • 43% of the exercise group reported exercising at home at least 2x weekly • Supervised only 1/week • Lost in follow-up: 43% of exercise group and 13% of control group

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
Bourke, 2014 [25] *Active treatment*	50 exercise intervention; 50 usual care	Adults with advanced prostate cancer on long-term ADT	Supervised aerobic and resistance exercise. Aerobic: 30 min at 55-75% of age-predicted max heart rate. Resistance: training of major muscle groups. Plus, weeks 1-6, do 1 self-directed exercise session; weeks 7-12, do 2 self-directed exercise sessions.	2x/wk for wks 1-6, once a wk in wks 7-12	One man in the intervention arm developed atrial fibrillation, and there was one death in the usual care arm. There were no skeletal-related adverse events during follow-up.	**QOL (FACT-P)** 12 wk mean difference and 6-mo mean difference. 12 wk: mean difference: 8.9 points; 95% CI 3.7 to 14.2; adjusted p=0.001 6 mo: mean difference: 3.3 points; 95% CI 2.6 to 9.3; adjusted p=0.27	• Adherence was 94% for the supervised exercise sessions • 82% of the prescribed independent exercise sessions over the first 12 wk.
Backman, 2014 [26] *Active treatment*	35 exercise intervention; 36 usual care	Adults with breast or colorectal cancer	To walk 10,000 steps/day. Plus 1 group walk 1 hour each week. Usual care group was provided with information on physical activity.	1x/day for 10 wks	Adverse events were not reported.	**QoL (EORTC QLQ-C30)** at baseline and 10 wks Exercise: 64.4 (SD=17.7); 59.1 (SD=18.2) Usual care: 62.9 (SD=19.1); 56.7 (SD=24.3) No significant difference between groups over time points, p=0.881	• 91% adherence average during intervention period • 74% completed exercise intervention • 34% reached the goal of 10,000 steps every week • EORTC QLQ –BR23 found a significant difference of p=0.045 between groups.

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
Arbane, 2014 [27] *Immediately post-operative*	64 exercise intervention; 67 usual care	Adults with NSCLC after curative surgery	1 30 minute cycle/day strength and mobility training days 1-5 post-op and home-based walking program with weekly telephone call to encourage continued 30 min of walking per day. Walking and strength training adapted to patient.	1x/day for 1-5 days; once home 1x/day -30 minutes walking for 4 wks	There were complications from surgery but no other adverse events were reported.	**QoL (SF-36 and EORTC QLQ-LC13)** scores No significant differences between groups from baseline to 4 wks after surgery. **Quadriceps strength** (kg force) A significant difference in muscle strength was found between the groups at the 4-week postoperative assessment (p=0.04). No other significant differences were found.	• The inpatient goals not met due to short stay or discomfort • Did an airflow obstruction sub analysis and found a significant difference between groups for QoL: p=0.01
Santa Mina, 2013 [29] *Active treatment*	32 aerobic exercise intervention; 34 resistance exercise intervention	Adults with prostate cancer receiving ADT	Moderate- to vigorous-intensity home-based sessions. Plus 1½ hour group-based booster sessions every other week (12 sessions). Aerobic group: any modality of aerobic exercise available at 60-80% maximum heart rate with progression (focused on walking). Resistance training group: 2-3 sets of 8-12 repetitions at an intensity of 60-80% one- repetition maximum, with resistance bands, exercise mat and stability ball.	30-60 minutes 3-5 days/wk for 6 mo	There were no serious adverse events related to exercise interventions beyond the expected muscle soreness associated with novel exercise.	**QoL (FACT-P)** Baseline and 6 mo scores Aerobic: 123.9 (SE=3.2); 124.2 (SE=3.2) Resistance: 119.3 (SE=3.6); 117.4 (SE=4.1) Difference between groups: p=0.935 **QoL (PORPUS)** Baseline and 6 mo scores Aerobic: 67.3 (SE=2.0); 65.8 (SE=2.1) Resistance: 62.2 (SE=2.0); 62.3 (SE=2.2) Difference between groups: p=0.625 **Aerobic capacity (VO_{2peak};** mL/kg/min) Baseline and 6 mo scores Aerobic: 25.1 (SE=1.8); 27.9 (SE=2.0) Resistance: 28.4 (SE=1.6); 30.5 (SE=1.6) Difference between group:	• Aerobic group attended 16.4% of booster sessions; 27 did not attend any. • Resistance group attended 5.5% of sessions; 22 did not attend any. • Log books not completed effectively • No control group • Small sample size

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
						p=0.565 **Grip strength (kg)** Baseline and 6 mo scores Aerobic: 63.9 (SE=2.6); 64.5 (SE=2.7) Resistance: 69.6 (SE=2.0); 68.9 (SE=2.3) Difference between group: p=0.865	
Rogers, 2013 [31] *Active treatment*	7 exercise intervention; 8 control group	Adults with head and neck cancer receiving radiation	Resistance exercise, 2 weekly supervised sessions for 6 weeks, 2 weekly home-based sessions. 9 different exercises using resistance bands increasing in repetitions and band thickness as strength increased.	1 hour 2x/wk for 12 wks	No serious adverse events occurred related to resistance exercise, but there were three unrelated ones.	**QoL (FACT-G)** scores at baseline, 6 and 12 wks Exercise: 73.8 (SD=14.8); 66.8 (SD=18.4); 70.6 (SD=18.2) Control: 90.4 (SD=10.8); 76.0 (SD=16.0); 84.6 (SD=13.8) Difference between groups: Baseline to 6 wks: 7.4 (SD=14.2), d=0.52 Baseline to 12 wks: 6.6 (SD=16.9), d=0.39	• Very small sample size
Midtgaard, 2013 [7] *Post treatment*	108 exercise intervention; 106 health evaluation program	Adults with cancer	Supervised progressive training high-intensity aerobic interval training and resistance training of major muscle groups. Plus counselling sessions. Goal was to have participants exercise at least 3 hours/week. Heath Evaluation Group had three, health evaluation session that included feedback following fitness testing and education on health	90 min 1x/wk for 12 mo	Six participants in the PACT group developed lymphedema, but continued to follow the progressive resistance training without exacerbation of symptoms.	**QoL (EORTC QLQ-C30)** Baseline and 12 mo mean Exercise: 67.21 (95% CI 62.70 to 71.56); 84.53 (95% CI 80.27to 88.36) Control: 67.16 (95% CI 62.65to 71.52); 81.17 (95% CI 76.78 to 85.19) Treatment Effect Ratio= 1.04 (95% CI 0.95 to 1.14), p=0.276 **Aerobic capacity (VO_{2peak};** mL/min) Baseline and 12 mo mean. Exercise: 1.97 (95% CI 1.89 to 2.05); 2.34 (95% CI 2.24 to 2.44) Control: 1.99 (95% CI 1.91 to 2.08); 2.28 (95% CI 2.18 to 2.38)	• Adherence to the weekly-supervised exercise training sessions was 66.6%. • Heart rate during supervised exercise sessions was 77 ± 7% of the measured heart rate maximum. • Significant improvements in physical activity in the control group • High attrition rate; 24% in control group; 32% in exercise group.

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
			benefits of regular exercise.			Treatment Effect Ratio= 1.04 (95% CI=1.00 to 1.07), p= 0.032 **Quadriceps strength (Leg Press kg)** Baseline and 12 month mean Exercise: 81.76 (95% CI 76.34 to 87.57); 109.68 (95% CI 101.98 to 117.97) Control: 84.54 (95% CI 78.89 to 90.60); 92.84 (95% CI 86.38 to 99.77) Treatment Effect Ratio: 1.22 (95% CI 1.15 to 1.30), p <0.001	
Lønbro, 2013 [42] *Post treatment*	20 early exercise intervention; 21 delayed exercise intervention	Adults with head and neck cancer after radiotherapy	30 progressive resistance training and self-chosen physical activity. Supervised 2-3 times, then left on own. Telephone calls every two weeks to deal with training related issues.	30 sessions in 12 wks	No adverse events were found.	**QoL (EORTC QLQ-C30)** Change in scores from baseline to 12 wks: Early exercise group: 19 (SD=14) Delayed exercise group: 6 (SD=12) Between group difference p<0.05	• Early: 17 of 19 patients returned their training logs. Based on these patients the mean training adherence rate was 91%. • Delayed: 10 of 15 patients returned their training logs. Based on these patients the mean training adherence rate was 98%.
Courneya, 2013 [33] *Active treatment*	96 aerobic exercise intervention (STAN); 101 high dose aerobic exercise intervention (HIGH); 104 combined aerobic and resistance	Adult women with breast cancer during chemotherapy	STAN: 75 min vigorous aerobic exercise per week HIGH: 150 minutes vigorous aerobic exercise per week COMB: 75 min vigorous aerobic exercise per week plus strength training program	All participants: duration of chemotherapy, start within 1-2 wks and end 3-4 wks after chemotherapy Aerobic	No serious adverse events were related to exercise.	**QoL (SF-36-general health),** Linear mixed -model analyses COMB vs. STAN Mean: −0.7, (95% CI −2.6 to 1.1); p=0.44; HIGH vs. STAN Mean: +0.6, (95% CI −1.2 to 2.5); p=0.50; HIGH vs. COMB Mean: +1.4, (95% CI −0.5 to 3.2); p=0 .14. **Aerobic capacity (VO_{2peak};** mL/kg/min) Linear mixed -model analyses	• Higher doses of exercise were achievable and safe.

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
	exercise intervention (COMB)			activity: 3x/wk, Strength training: 3x/wk		COMB vs. STAN Mean: −0.2, (95% CI −1.2 to 0.8); p=0.70; HIGH vs. STAN Mean: +0.9, (95% CI −0.1 to 1.9); p=0.08; HIGH vs. COMB Mean: +1.1, (95% CI 0.1 to 2.1); p=0 .03. **Quadriceps strength (Leg Press -kg)** Linear mixed –model analyses COMB vs. STAN Mean: +6.0, (95% CI 1.4 to 10.7); p=0.01; HIGH vs. STAN Mean: +0.0, (95% CI −4.6 to 4.6); p=0.99; HIGH vs. COMB Mean: -6.0, (95% CI -10.7 to -1.4); p=0.01.	
Cormie, 2013 [5] *Post treatment*	22 high-load resistance exercise intervention; 21 low-load resistance exercise intervention; 19 usual care	Adult women with breast cancer-related lymphedema	6-10 repetition maximum (75-85 % of one repetition maximum [1RM]) for the high-load group or from 15-20 repetition maximum (55-65 % 1RM) for the low-load group. Usual care group was offered an exercise program after study completion.	1 hour, 2x/wk for 3 mo	No lymphedema exacerbations or other adverse events occurred.	**QoL (SF-36-MCS)** Change in scores High-load Exercise: 2.9 (SE=1.7) Low-load Exercise: 6.6 (SE=1.6) Usual care: 1.7 (SE=1.7) No significant difference between groups, p=0.195. Significant difference between exercise groups and usual care for muscle endurance for chest press and seated row but not leg press and grip strength-affected arm.	• Change to the extent of swelling across the 3-month intervention did not differ between groups • Significant difference between groups for SF-36 -physical function

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
Cormie, 2013 [44] *Post treatment*	10 exercise intervention; 10 usual care	Adults with prostate cancer with bone metastases	Resistance-based exercises of major muscle groups with an exercise specialist in groups of 1-5. Usual care group was offered an exercise program after study completion.	1 hour, 2x/wk for 12 wks	No adverse events or skeletal complications occurred during the supervised exercise sessions.	**QoL (SF-36-MCS)** Baseline and 3 mo scores Exercise: 44.1 (SD=10.1); 42.6 (SD=12.9) Usual care: 43.5 (SD=7.2); 43.9 (SD=11.4) No significant difference between groups, p=0.475	• High attendance (83%) and compliance rates (93%)
Broderick, 2013 [45] *Post treatment*	23 exercise intervention; 20 usual care	Adults with cancer who completed therapy 2-6 months preceding	Aerobic-based group sessions plus home exercise program. Working up to 75% heart rate reserve. Incremental increases in time for brisk walking at home 3-5x/wk. Usual care group was offered an exercise program after study completion.	2x/wk plus brisk walking for 8 wks	No adverse events were found.	**QoL (FACT-G total score)** at baseline, 2 and 3 mo, respectively Exercise: 86.2 (SD=14.8); 90.0 (SD= 12.5); 92.1 (SD=14.0) Usual care: 91.6 (SD=7.5); 95.4 (SD=11.3); 93.3 (SD=19.0) No significant difference between groups at time points, p=0.94, p=0.37 **Aerobic capacity (VO_{2peak};** mL/kg/min) at baseline, 2 and 3 mo, respectively Exercise: 19.7; 24.1; 22.8 Usual care: 19.1; 20.2; 20.4 No significant difference between groups at time points, p=0.14, p=0.61	• 60.9% attended > 70% of group exercise classes • 78.3 % met home exercise program guidelines • Participants had very low fitness levels at start
Andersen, 2013 [34] *Active treatment*	106 exercise intervention; 107 wait-list control	Adults with cancer receiving chemotherapy	4.5 hours high intensity training (cardio and heavy resistance) 1.5 hours body awareness 2 hours relaxation 1 hour massage Usual care group was offered an exercise	9 hours/wk for 6 wks	Adverse events were not reported.	**QoL (FACT-G score)** No significant difference between exercise and wait-list control group, p=0.21	• Self-referral of participants who were motivated to participate in group-based physical activity. • Adherence was 75%

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
			program after study completion.				
Stigt, 2013 [28] *Active treatment*	23 exercise intervention; 26 usual care	Adults with NSCLC 4 wk after thoracotomy	Cycling between 60%-80% of peak cycling load plus muscle training.	1 hour 2×/wk for 3 mo	Adverse events were not reported.	**QoL (SF-36, general health)** No significant difference between exercise and usual care groups **Aerobic capacity (6MWT)** Exercise: 35m increase Usual care: 59m decrease Significant difference between groups, p=0.024	• High dropout rate • Conclusion: waiting 3-4 mo may be better • Increase in exercise tolerance caused more pain and physical limitations • In exercise group, only 33% of patients on ACT completed the program, whereas 83% of patients not on ACT completed it
Samuel, 2013 [30] *Active treatment*	24 exercise intervention; 24 usual care	Adults with head and neck cancer receiving chemo-radiotherapy	Brisk walking 15-20 min at 3-5 RPE and active weight program for major muscle groups of upper and lower limbs at 3-5/10 RPE; 8-10 reps for 2-3 sets.	5×/wk for 6 wks	No adverse events were found.	**QoL (SF-36-MCS)** Exercise: 11.73% increase Usual care: 75.21% decrease Significant difference between groups, p<0.001 **Aerobic capacity (6MWD)** Exercise: 42m increase Usual care: 96m decrease Significant difference between groups, p<0.001	• Adherence not measured
Pinto, 2013 [41] *Post treatment*	20 exercise intervention; 26 usual care	Adults diagnosed with stage I-III colorectal cancer	Weekly calls, PA counselling, home logs, and a pedometer; then monthly calls for 3 mo Start 10 min for 2 days/wk to 30 min/day for 5 days/wk of brisk walking or use of home exercise equipment at 64%-76% of estimated max heart rate	Start: 2×/wk End: 5×/wk for 12 wks	Adverse events were not reported.	**QoL (FACT-C score),** at baseline, 3, 6, and 12 mo, respectively Exercise: 105.3; 111.3; 111.7; 110.7 Usual care: 105.3; 110.8; 108.7; 110.6 No significant difference. **Aerobic capacity (VO_{2peak};** mL/kg/min) at baseline, 3, 6, and 12 mo, respectively Exercise: 22.97; 27.65; 28.43;	• 7-day physical activity recall showed exercise group did significantly more exercise than usual care group at 3 mo but not at 6 and 12 mo • No real exercise program • Primary outcome was increase in physical activity with an

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
			Assessments at baseline, 3, 6, and 12 mo.			27.06 Usual care: 22.97; 23.71; 24.36; 22.12 Significant difference between groups at time points; at 3 mo, p=0.017; at 6 mo, p=0.017; and at 12 mo, p=0.002	emphasis on behavioural counselling
Hayes, 2013 [32] *Active treatment*	67 exercise group with face-to-face support; 67 exercise group with telephone support; 60 usual care	Adult women diagnosed with breast cancer 6 wk post-surgery	Individually tailored program 16 sessions (in person or via telephone) with exercise physiologist weekly then tapered to monthly Wk 1-4: aerobic, low-to-moderate intensity, 20-30 min Wk 5-8: aerobic with strength introduced, moderate intensity, 30-40 min Wks 9-32: aerobic and strength, moderate to high intensity, ≥45 min Measures taken at pre-intervention (5 wks), mid-intervention (6 mo) and post-intervention (12 mo post-surgery).	By end of program: ≥45 min 4×/wk using both aerobic exercise and strength-based exercise at least 2×/ wk for 8 mo	No adverse effects, events, or lymphoma were found.	**QoL (FACT-B+4 scale),** score change from baseline to 12 mo post-surgery Exercise (face-to-face): +9.5 (95% CI 5.3 to 3.8) Exercise (telephone): +13.5 (95% CI 10.0 to 17.0), p≤0.05 Usual care: +6.5 (95% CI 1.8 to 11.1) Face to face and telephone group had clinically meaningful change over time. Significant between-group differences in QoL between telephone group and usual care group (p≤0.05) **Aerobic fitness (modified 3-min step test)** change in heart rate from baseline to 12 mo post-surgery Exercise (face-to-face): -9.0 (95% CI -12.9 to -5.2), p≤0.05 Exercise (telephone): -6.3 (95%CI -10.2 to -2.4), p≤0.05 Usual care group: +2.7 (95% CI -3.0 to 8.4) Face-to-face group had clinically meaningful change over time. Significant differences were found between the face-to-face and telephone groups compared	• 88% of face-to-face group and 81% of telephone group completed scheduled sessions with exercise physiologist • 25% in face-to-face and telephone groups did not meet intervention goal of increasing total physical activity between measures • 66% of women in usual care group participated in ≥180 min of activity/wk and/or increased activity by 30 min/wk

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						with the usual care group, p≤0.05 **Upper body function strength and endurance test (kg)** at baseline and 12 mo: Exercise (face-to-face): 7.3 (95% CI 6.7 to 7.9); 9.2 (95% CI 8.6 to 9.8) Exercise (telephone): 6.8 (95% CI 6.1 to 7.5); 8.3 (95% CI 7.8 to 8.8) Usual care: 6.3 (95% CI 5.4 to 7.2); 8.0 (95% CI 7.1 to 9.0) All are statistically significant different for time and group effect, p<0.05	
Ergun, 2013 [43] *Post treatment*	20 supervised exercise; 20 home exercise; 20 education only	Adult female breast cancer patients	Exercise (supervised): aerobic exercise + resistive exercise (upper and lower limb exercises with Theraband, moderate intensity and brisk walking under the supervision of a specialist doctor) Exercise (home): brisk walking at home, moderate intensity + weekly phone calls Assessed before and after program.	Group 1: 45 min, 3×/wk for 12 wks plus brisk walking for 30 min/day, 3x/wk for 12 wks Group 2: 30 min; 3×/wk for 12 wks	No adverse effects, events or safety failures were found.	**QoL (EORTC QOL-C30)** at baseline and 12 wks Exercise (supervised): 67.91 (SD=16.5); 74.16 (SD=18.7); p=0.038 Exercise (home): 61.24 (SD=23.3); 68.97 (SD=21.2); p=0.489 Control (education): 74.58 (SD=23.5); 67.9 (SD=16.7); p=0.265 No significant difference between groups, p=0.085	• All groups received a 30-min education program • Primary objective: to look at angiogenesis and apoptosis-related molecules
Yeo, 2012 [35] *Active*	54 exercise intervention; 48 usual care	Adult patients with pancreatic and periampullary	Every Step Counts - home walking program Monthly diary and	3-5×/wk for 3 mo	Adverse events were not reported.	**QoL (SF-36-MCS),** Baseline and 3 mo scores Exercise: 45; 51 Usual care: 44; 48	Adherence not measured

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
treatment	79 completed study at final follow-up at 19 mo	cancer	monthly phone call Warm up, brisk walking, cool down: Mo 1: 5, 10, 5 min Mo 2: 5, 20, 5 min Mo 3: 5, 25-30, 5 min Low-to-moderate intensity.			Significant difference between groups, p≤0.05	
Schmidt, 2012 [46] *Post treatment*	15 exercise intervention; 18 usual care	Adult breast cancer patients	Exercise group: strength endurance training based on training load of hypothetical maximum force test (h1RM) was set at 50% and a training plan was developed for each participant with 20 reps during 1 training set/device (11 devices) Usual care group: weekly conventional gymnastics exercises, such as chair or floor exercises Assessments at study entry, 3, 6 mo.	1 hr 1×/wk for 6 mo	Adverse events were not reported.	**QoL (EORTC QLQ C30) at baseline, 3 mo and 6 mo scores** Exercise: 59 (SD=16.6); 67 (SD=19.9); 76 (SD=12.9); p<0.01 Usual care: 67 (SD=17.2); 75 (SD=18.0); 77 (SD=15.3); p<0.01 No significant difference between groups.	Usual care group in this study used conventional exercise gymnastics
Saarto, 2012 [47] *Post treatment*	263 exercise intervention; 237 usual care	Pre- or post-menopausal breast cancer survivors	12-mo step aerobics and circuit training – BREX; supervised sessions -60 min (1×/wk) and home (2×/wk) RPE: 14-16 or ~86%-92% HR_{max} or 76%-85% of VO_{2max} and 5-7 METs	60 min 3-4×/wk for 12 mo	Adverse events were not reported.	**QoL (EORTC QLQ-C30),** score change from baseline to 12 mo Exercise: 4.2 (95% CI 1.9 to 6.6) Usual care: 5.6 (95% CI 3.1 to 8.1) No significant difference between groups, p=0.43 **Aerobic capacity (2MWT; m),** difference from baseline to 12	• Adherence: 62% for supervised weekly training sessions • 88% trained mean 3.2 hr/wk • Median number of training sessions was 3.8/wk • Very active usual care group; therefore, no difference between

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
						mo Exercise: -0.89 (95% CI -1.03 to -0.76) Usual care: -0.72 (95% CI -0.85 to -0.58) No significant difference between groups, p=0.15 For all participants, significant linear trend between higher physical activity (increase in METs/wk) and improved QoL, p=0.011	groups • The exercise group increased physical activity by 3.10 MET-h/wk • The usual care group increased by 3.57 MET-h/wk (~17%); increases similar in both groups (p=0.97); all participants were also very active before study • Not sensitive enough questionnaire (for patients not survivors)
Eakin, 2012 [36] *Active treatment*	68 exercise intervention; 69 usual care	Women with invasive breast cancer	16 calls with exercise physiologist of 15-30 min 0-2 mo: 1×/wk 2-4 mo: 1×/2 wk 4-8 mo: 1×/mo Target: 45 min, moderate-to-vigorous aerobic activity + strength-based exercise at least 2×/wk; Exercise workbook provided. Assessments at baseline, 6 and 12 mo post-surgery.	45 min 4×/wk for 8 mo	No serious adverse events, but 2 minor events due to muscle soreness and 1 musculo-skeletal injury.	**QoL (FACT-B+4;** score range 0-160), mean change difference 12-mo post-surgery Exercise group with telephone calls vs. usual care=3.7 (95% CI -1.5 to 8.9), p=0.156	• For telephone group, there was a median of 14 calls with exercise physiologist; 79% completed majority (>75%) of calls • Change from baseline to 12-mo post-surgery clinically meaningful in QoL and upper body function for exercise group only
Anderson, 2012 [3] *Post treatment*	52 exercise intervention; 52 usual care	Adult women with stage I-III breast cancer	RESTORE: centre-based moderate tailored exercise program 0-3 mo: 2×/wk for 60	65 min 2×/wk for 12 mo	39 adverse events; 7 serious, but only 2 events were deemed	**QoL (FACT-B score),** mean at baseline and 18 mo Exercise: 102.6 (SD=16.9); 115.8 (SD=1.6) Usual care: 103.7 (SD=22.1); 114.4 (SD=2.5)	• Primarily examined exercise-induced lymphedema • 71.2% of participants completed all

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
			min; 20 min resistance training and 30 min walking 4-6 mo: option for home-based, 1×/wk at centre 7-12 mo: exercise at home or facility Assessments at baseline, 6, 9, 12, 15, and 18 mo.		study-related (pectoral muscle pain and stress fracture in foot).	No significant differences between groups, p=0.57 **Aerobic capacity: (6MWT; m),** mean at 18 mo Exercise: 593.2 (SE=13.0) Usual care: 558.9 (SE=11.8) The exercise group walked significantly further, p=0.0098	prescribed sessions (0-97%) • 61% of participants attended more than 75% • 13% attended <50% of sessions
Arbane, 2011 [37] *Immediately post-op*	27 exercise intervention; 26 usual care	Adults with NSCLC referred for lung resection via open thoracotomy or visual-assisted thoracotomy	2×/day strength and mobility training days 1-5 post-op and 12-wk home-based program with 3 visits (1×/mo) to encourage continued use of exercise program Walking and strength training adapted to patient. 60%-80% of maximal heart rate.	5-10 min to start then adapted to individual 2×/day for 5 days post-surgery, then for 12 wks	Adverse events were not reported.	**QoL (EORTC-C30, global health score),** 12-wk change Exercise: 6.5 (95% CI –7.7 to 20.7) Usual care: 2.2 (95% CI -5.2 to 9.6) No significant difference over time or between groups **Aerobic fitness (6MWT; m),** mean at pre, 5-day postoperative and 12-wk follow-up, respectively Exercise: 466.6 (SD=102.1); 336.7 (SD=84.1); 480.2 (SD=110.0) Usual care: 455.7 (SD=98.0); 308.7 (SD=124.8); 448.2 (SD=95.1) Repeated measures analysis: Overall: within-subjects time effect, p<0.001; group effect, p=0.47 From preoperative to 5 day post-op (paired t tests):	• No adherence information • No clear intervention information after 5-day postoperative • Some loss to follow-up • Many participants could not do quad strength measures because of metal implants and many did not do the quad strength measures again

Author	Sample size	Population, diagnosis	Intervention	Frequency and duration	Adverse events	Main findings	Comments
						between-subjects group time effect, p=0.89 **Quadriceps strength (magnetic stimulation of femoral nerve; kg),** mean at pre, 5-day postoperative and 12-wk follow-up, respectively Exercise: 33.2 (SD=15.2); 37.6 (SD=27.1); 34.2 (SD=9.4) Usual care: 29.1 (SD=10.9); 21.5 (SD=7.7); 26.4 (SD=9.7) Repeated measures analysis: within-subjects time effect, p=0.70 For preoperative and 5-day postoperative between-subjects group effect, p=0.04	

Abbreviations: ADT: androgen deprivation therapy; EORTC C-30: European Organization for Research and Treatment of Cancer; EX: exercise group; FACT-B: Functional Assessment of Cancer Therapy – Breast; HR: heart rate; HRQoL: health-related quality of life; min: MCS: mental component summary; minute; MET: metabolic equivalents; MWT: minute walking test; mo: month; PACT: Physical Activity after Cancer Treatment; pt: patient; PORPUS: patient oriented prostate utility scale; RCT: randomized controlled trial; RPE: rate of perceived exertion; RT: resistance training exercise; QoL: quality of life; SF-36: Short Form (36) Health Survey; UC: usual care; VO_2: volume of oxygen; vs: versus; wk: week

DISCUSSION

The interpretation of the systematic reviews and RCTs evaluating exercise benefits in people with a previous or current diagnosis of cancer is complex. There are many different exercise interventions, types of cancer, cancer treatments, phases or timing of delivery, assessment measurements, and outcomes that need to be considered.

The objective of this guideline was to provide guidance for oncologists, exercise consultants, primary care providers, and other members of healthcare teams, such as (but not limited to) physiotherapists, social workers, psychologists, nurses, and occupational therapists, about exercise for people having been treated for, or living with, cancer and try to provide specific recommendations with regard to type of exercise, pre-exercise assessment requirements, and addressing safety concerns.

The evidence indicates that exercise can provide QoL and fitness benefits for adults living with cancer, whether they are on active treatment or post-treatment. During active treatment, systematic reviews examining patients with all cancers demonstrated a positive influence of exercise on QoL. RCTs found benefits within and between groups for exercise interventions of moderate intensity. For the post-treatment period, systematic reviews found a positive influence for all exercise interventions. Exercise may also help prevent deconditioning that occurs during cancer treatment because exercise improves muscular fitness but the data are not included in this guideline. The guideline focused on studies during and post treatment.

Unfortunately, there was no RCT evidence examining the effects of exercise on survival. It is important to recognize that there is no RCT evidence that exercise will improve or worsen a patient's chances for longer survival or a treatment of cancer. The benefits of exercise are limited to QoL and aerobic and muscular fitness. More research into the area of exercise and survival should be a priority.

Safety

The research supports that it is safe for people with all types of cancer to exercise while on treatment or after completion of treatment. The safety of exercise training both in active and post-treatment was concluded in the guidelines from the Belgian Health Care Knowledge Centre [2] and the ACSM [1]. There were minimal adverse events reported in the systematic reviews and RCTs. However, only participants considered medically stable enough to exercise were eligible for these trials.

Pre-screening considerations before exercising is an important issue to ensure the exercise regimen is suited for a specific person with cancer. CPET, a validated screening tool, was found to be safe for all people with cancer.

The ACSM developed some cancer site–specific medical assessments that should be addressed before exercising that can be found in Appendix 7 [1]. They suggest assessing the morbidities, treatments, metastases sites, cancer site–specific issues, and the types of exercise for people with cancer wanting to exercise. In their guideline, there are references to research that provide more in-depth information for developing pre-exercise assessments.

Exercise Type

The Belgian Health Care Knowledge Centre found no conclusive evidence that allowed for a recommendation in favour for a particular exercise intervention [2]. There were no systematic reviews that compared one type of exercise with another and most interventions had both aerobic and resistance components. Resistance exercise improved QoL in those systematic reviews that evaluated only resistance exercise and demonstrated increases in muscular strength [10,12,49]. There were no systematic reviews that analyzed only aerobic

exercise and QoL. However, bivariate moderator analyses found that increases in aerobic activity intensity also increased QoL [11].

In the RCTs, most used a combination of both aerobic and resistance exercise intervention [3,7,23-25,27,28,30,32-34,36-40,42,43,46,47]. One RCT compared a resistance exercise intervention with an aerobic exercise intervention and found no difference between groups for QoL [29].

There was little evidence that demonstrated a superior outcome for a certain frequency, duration, or intensity to support a recommendation to create a specific regimen. There were no direct comparisons of these domains and the range of all these domains was very large. There is some evidence to support that longer time periods and greater amounts of aerobic activities as measured in METs (6-8 METs) increased the efficacy of the intervention [4,11,18,54], although there may be a limit to this benefit because an inverse dose-response was also found.

The group turned to the CSEP Canadian Physical Activity Guidelines [54] as a basis for an exercise program for people with cancer. As a minimum guideline, individuals should exercise for at least 150 minutes per week at a level of moderate-intensity aerobic physical activity, in bouts of 10 minutes or more. The panel believed that some small modifications to these guidelines would provide the best guidance for people with cancer and would match with the evidence for length and intensity while still allowing for individuals to choose an exercise of their liking. CSEP also includes flexibility activities three to four times per week in their guidelines, which may also be helpful but were out of the scope of this guideline. The ACSM also developed person-specific exercise modifications for various cancer types, which can be found in Appendix 8, but based their basic recommendations on the age-specific Physical Activity Guidelines for Americans [1].

There is also evidence to support the statement that exercising in a group setting and/or with supervision might provide a superior benefit to home-based exercise [11,19]. An exercise program that may help groups considering creating their own cancer-specific exercise program may want to refer to the following manual for assistance in cancer-specific issues and exercise: Active Living for Older Adults in Treatment for Cancer.

Cancer Type

There were identified systematic reviews/studies on breast, prostate, lung, colorectal, head and neck, bladder and HSCT patients, but the evidence in those articles does not affect the basic recommendation for exercise. No systematic reviews/studies were identified on any other site, but the available evidence gives no cause to think that people with other cancers would not benefit from exercise unless the specific nature of the cancer would preclude exercise.

Interventions with women with breast cancer tended toward aerobic exercise. Lymphedema has been an issue for women with breast cancer and most allied health professionals who treat or care for these patients. Importantly, there is clear evidence that not only will exercise NOT precipitate lymphedema in women with breast cancer, but also those women who already have lymphedema can still safely exercise and improve their lymphedema, QoL, and fitness. Women with breast cancer, including those with lymphedema, can safely engage in moderate amounts of exercise while on active treatment or post completion of treatment [3-7].

Trials in the setting of prostate cancer were mostly with men on ADT [12,14,22,23,25,29,44]. Whether in the hormone-sensitive metastatic or high-risk locally advanced, it was found that exercise could be safely performed with benefits in QoL, muscle mass, and strength [12,14,18,22,23,25,29,44].

Evidence Limitations

The panel wanted to create specific exercise regimens for each type of cancer based on evidence. The evidence was not available for this. As well, there was insufficient evidence that met the inclusion criteria to provide recommendations based on survival outcomes.

Some evidence used in this guideline did not have QoL, fitness, or safety as primary endpoints but as a secondary one. The guideline from the ACSM was not a systematic review and was dependent on expert opinion for some topics such as their pre-screening guidelines.

Many of the systematic reviews had issues with heterogeneity in their analysis. Sources of heterogeneity included patients with different cancer types; timing of the exercise intervention (during or post completion of therapy); different interventions (aerobic versus resistance); different lengths of intervention (four to 24 weeks); variable intensities; frequency of interventions (daily to two, three, or five times per week); multiple measures of QoL, aerobic capacity, and strength; and interventions with individual or group sessions and the timing of the assessments.

The risk of bias in lifestyle trials is an acknowledged issue. Within the RCTs reviewed, the following concerns were noted: the participants could not be blinded, some assessments (especially QoL) were subjective, many trials had performance bias, many did not measure exercise activity before entry into the study, adherence during the intervention was variable or not reported, and the exercise levels of the control group quite often increased during the intervention, sometimes as much as the exercise group. RCTs are not long enough to really study long-term duration of exercise. The study length had more to do with amount of money and time to complete study as opposed to the feasibility or sustainability of an exercise regimen.

CONCLUSIONS

Exercise provides benefits in QoL and muscular and aerobic fitness for people with cancer both during and post treatment, and does not cause any harm. There is sufficient evidence to promote exercise among adults with cancer and some evidence to promote exercise in a group or supervised setting and for a long period of time to improve their QoL and muscular and aerobic fitness. It is important to have a pre-screening assessment to evaluate for effects of disease, treatments, or comorbidities. More research would be beneficial to help create more exact exercise programs for specific cancer types. However, recommendations consistent with the CSEP Canadian Physical Activity Guidelines allows for flexibility in order for people with cancer to perform the mode of exercise they may prefer.

CONFLICT OF INTEREST

Information regarding conflict of interest declarations can be found in Appendix 1.

Guideline 19-5: Section 5

Exercise for People with Cancer: Internal and External Review

INTERNAL REVIEW

The Guideline Development Group (GDG), Expert Panel and the Program in Evidence-Based care (PEBC) Report Approval Panel (RAP) (Appendix 1) evaluated the guideline. The results of these evaluations and the Working Group's responses are described below.

Expert Panel Review and Approval

Of the 14 members of the Exercise for People with Cancer Guideline Development Group, 12 members cast votes and two abstained, for a total 86% response. Of those who cast votes, 12 approved the document (100%). The main comments from the Expert Panel and the Working Group's modifications/actions/responses made in response are summarized in Table 1.

Table 1. Modifications/actions/responses regarding main comments from the Expert Panel.

Main comments	Modifications, actions, or responses
1. Add kinesiologists to the intended users.	The Working Group added kinesiologists to the intended users list.
2. I do not think survival evidence can be ignored. It may not be the best, but it is there.	The Working Group acknowledged that survival is important, but felt that until there were RCTs, non-RCT data are not robust enough to add to the guideline.
3. Perhaps merge recommendations 6 and 7 together.	The Working Group merged recommendations 6 and 7 together.

Report Approval Panel Review and Approval

Three RAP members reviewed this document in December 2014. The RAP approved the document December 15, 2014. The summary of main comments from the RAP and the Working Group's modifications/actions/responses made in response are presented in Table 2.

Table 2. Modifications/actions/responses regarding main comments from the Expert Panel.

Main comments	Modifications, actions, or responses
1. If there is an RCT in which the within-exercise group analysis showed a benefit over time but there were no between-group effects – then this is NOT evidence of benefit because of exercise. Without a between-groups effect, there is no evidence of exercise conferring a benefit.	The Working Group removed the group analyses from the results sections unless the study had a priori planned with repeated measures analysis.
2. Discuss the survival issue and the lack of RCT evidence.	The Working Group added a paragraph in both the Results and the Discussion sections reflecting the lack of RCT exercise intervention and survival evidence.
3. Remove qualifying statements since because those particular groups were not a part of the original questions.	The Working Group removed the qualifying statements.

EXTERNAL REVIEW

External Review by Ontario Clinicians and Other Experts

Targeted Peer Review

Eight targeted peer reviewers from Ontario who are considered to be clinical and/or methodological experts on the topic were identified by the Working Group and the Expert Panel. Six agreed to be the reviewers and five responses were received. Their affiliations and conflict of interest declarations are in Appendix I. Key results of the feedback survey are summarized in Table 3. The main written comments from targeted peer reviewers and the Working Group's modifications/actions/responses are summarized in Table 4.

Table 3. Responses to nine items on the targeted peer reviewer questionnaire.

	Reviewer Ratings (N=5)				
Question	Lowest Quality (1)	(2)	(3)	(4)	Highest Quality (5)
1. Rate the guideline development methods.	0	1	1	1	2
2. Rate the guideline presentation.	0	0	2	2	1
3. Rate the guideline recommendations.	0	1	2	1	1
4. Rate the completeness of reporting.	0	0	1	2	2
5. Does this document provide sufficient information to inform your decisions? If not, what areas are missing?	0	0	3	0	2
	Strongly Disagree (1)	(2)	Neutral (3)	(4)	Strongly Agree (5)
6. Rate the overall quality of the guideline report.	0	0	2	1	2
7. I would make use of this guideline in my professional decisions.	1	0	1	1	2
8. I would recommend this guideline for use in practice.	0	0	2	1	2
9. What are the barriers or enablers to the implementation of this guideline report?	Some of the targeted peer reviews felt that barriers include a lack of: funding, facilities, programs, qualified staff and exercise specialists in cancer. As well, the lack of knowledge of exercise in clinicians/healthcare professionals and having pre-exercise screening for all cancer survivors would also be barriers.				

Table 4. Modifications/actions/responses regarding main written comments from targeted peer reviewers.

Main written comments	**Modifications, actions, or responses**
1. The composition of the Expert Panel has modest representation of exercise professionals.	The Working Group feels that the expert panel has expertise in exercise and oncology. We will add more qualifications to Appendix 1 to better inform the reader.
2. Type of evidence and measures Use of self-report data vs objective outcomes –self-report now considered not accurate when discussing intensity/volume outcomes. Further, objective data (not self-report) are demonstrating that survivors' post-primary therapy are far below population norms for	The Working Group feels that the objective of the guideline was to study exercise and QoL and QoL is a self-report measure. The Working Group also feels that "improve muscle mas means that regardless of ones starting point, the individual will increase the amount of muscle they have.

	physical functioning. At this low level, they are at increased risk of comorbidity. Yet, the guidelines do not emphasize the importance of exercise to counter the treatment-induced deconditioned state of cancer patients. The word choice is interesting, as it does not highlight this. Most individuals do not understand that 'improve muscle mass' means "your muscle mass is below norm, predisposing you to increase risk of falls, fracture, decreased QOL etc". If the group compares objective measures to population norms/healthy norms, cancer survivors are then categorized at higher risk for future disease development.	The Working Group will as add in the discussion that exercise may help prevent deconditioning because exercise improves muscular fitness but the data to support this are not included in this guideline.
3.	Better define "moderate amount"	The Working Group added *(See Recommendation 3)* to Recommendations 1 and 2 to help quantify moderate amount immediately.
4.	QoL as outcome & define better & what was not included and why? No mention of exercise effects on symptoms, body composition, or other important outcomes. It would be useful to address some of the psychosocial benefits of physical activity such as anxiety, depression, mood.	The Working Group would like to emphasis that the objective of the guideline was to study whether exercise had an influence on QoL and did examine the effect of exercise on muscular strength and aerobic capacity. There is a CCO guideline examining depression. The Working Group added a definition for QoL in the introduction.
5.	It might be beneficial to address the benefits of exercise across the cancer care trajectory (i.e, pre-treatment, during treatment, survivorship, palliative care).	The studies included in the guideline were trials on active and post treatment. The other phases are important but weren't searched for and there were no studies that covered the whole cancer trajectory. The Working Group added in the discussion section what types of information was focused on in the guideline.
6.	There is some inconsistency with both the terms 'strength training' and 'resistance training' used interchangeably (e.g. pg 4). It would less confusing for audiences not familiar with exercise if one or the other term was used consistently (preferably resistance training)	The Working Group agreed and changed *strength training* to *resistance training*.
7.	Based on the Working Groups' criteria, guidelines were justified by sig or non-significance, but it should be noted many times significant differences are not determined because the research group either used self-report, or did not follow the basic principles of exercise training, so cancer treatment side effects were not attenuated.	The objective of the guideline was to study exercise and QoL and QoL is a self-report measure. The Working Group did emphasis the limitations of the studies and tried to put the significance of the data into context of those limitations.
8.	I felt that the guidelines were somewhat general and might be difficult to follow for clinicians/healthcare professionals who may not be experts in PA and require more guidance in exercise prescriptions. It would be useful to have examples of starting intensities for patients up front in the 'recommendations summary.'	The Working Group realizes that more guidance would be preferable but that the data did not supply enough information to be more exact. The patient's personal preferences and fitness levels will also play a role in their exercise routines. The Working Group will add a link to an existing exercise program for cancer patients in the discussion. http://www.alcoa.ca/e/cancer_project/pdf/alcoa_exercise_manual.pdf
9.	Should include some information for flexibility training and should also address other	The Working Group recognizes that flexibility is important but the definition of exercise used in this guideline was

	alternative forms of exercise such as yoga.	any *physical activity resulting in an increase in energy expenditure and involving 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 outcomes* [1] and so we feel we can't really make recommendations regarding yoga or alternate forms of exercise. However, the CSEP guidelines do include flexibility and we will add that into the discussion. "Finally, it is recommended that adults engage in flexibility activities 3-4 times per week. Incorporating activities that improve flexibility into habitual activity may improve mobility and functional independence as well as reduce the risk for falls."
10.	Add note on detriments of inactivity? Although we would like cancer patients undergoing treatment to meet the exercise guidelines, there should also be a statement to avoid inactivity during this period and to exercise as much as tolerated given that some treatment regimes are more difficult than others. It is surprising that there is no "it's never too late to start" message given the evidence, and this would be important for clinicians to understand	The Working Group feels that this issue is discussed in the last paragraph of the preamble.
11.	Would it be useful to include in the label on screening guidelines a word that indicates this section outlines safety considerations (or special considerations)? I would think practitioners would be especially interested in seeing a section on precautions. Additionally, is there any information that can be added on about resistance training and PICC lines (a question I encounter frequently from practitioners and patients).	The Working Group feels this issue is met in the ACSM guidelines in Appendix 8. To ensure people are aware of that information we will make reference to the ACSM guideline in the preamble and discussion.
12.	Did the developers consider a section on motivation and behaviour change? Or is the message to clinicians "good luck with getting patients on chemo to exercise"? How was behavioural counselling in the studies used as evidence? How many of the reviews and RCTs include behavioural counselling? This is a major oversight and limitation of the recommendations as currently presented.	Motivation and behavioural change were not a part of the objectives of this guideline.
13.	Some further insight into the specifics of the recommendation that exercise should be done in a group is warranted. What is it about the group? How many people make up a group? Is it simply the supervision, or the group members? This is a novel and important recommendation and more specifics would be helpful to those using the guideline.	Unfortunately, the evidence did not provide much information on which type of group might be better than another. Paktakia [15] found that programs that improved QoL all were gym-based and under the supervision of a physiotherapist. Using a physiotherapist might result in regular monitoring, program adherence, support and encouragement but its costs. Using a gym can provide social interaction but can cost and can be intimidating.
14.	It would be helpful to see the "how" and "what" involved in pre-screening and fitness assessments.	The Working Group feels this issue is met in the ACSM guidelines in Appendix 7. To ensure people are aware of that information we will make reference to the ACSM guideline in the preamble and discussion.

15. There is no comment on following exercise training principles and the need for progression/change to continue health maintenance/improve further health outcomes. General word choice changes in this document could improve this.	The Working Group feels that this is not within the scope of the guideline. In the preamble, we say that those people with cancer who may not meet the guidelines have room to improve and work up to the recommendations that we state. These guidelines are not intended to provide exercise specialists with specifics about how to implement an exercise training program for people with cancer. That is far beyond the scope of an oncologist's or primary health care provider's practice. There are special training courses offered by professional exercise training organizations for kinesiologists or exercise specialists to take that "certify" them to design these programs; putting all of those details into these guidelines is far beyond the scope of the guideline and how these guidelines will be applied.
16. Are the CCO guidelines about patients and improving standard of care for the best health outcomes, or about inter-country or inter/intra-society political fights? There is no evidence that CSEP recommendations provide appropriate guidelines for a cancer survivor to attain a "healthy" norm.	The Working Group feels this is not relevant to the objectives and questions of this guideline.
17. My major concern is that this will be published in 2015, but by 2017 it may be obsolete. As so much came out in 2014, I highly suggest 2014 evidence be included in the guidelines so the recommendations can be used for many years to come, and not have to be revisited by 2017.	All PEBC documents are maintained and updated through an annual assessment and review process.

Professional Consultation

Feedback was obtained through a brief online survey of healthcare professionals and other stakeholders who are the intended users of the guideline. All medical and radiation oncologists, nurses, nurse practitioners and family practitioners in primary care in the PEBC database were contacted by email to inform them of the survey. Five hundred and thirty-six were included; 529 were located in Ontario including two from Quebec, one from New Brunswick, one from Alberta, one from British Columbia, one from Maryland and one from Australia. Sixty-nine (13%) responses were received. Four hundred sixty-seven stated that they did not have interest in this area or were unavailable to review this guideline at the time. The key results of the feedback survey from 69 people are summarized in Table 5. The main comments from the Professional Consultation that were different than the Targeted Peer Reviewers comments and the Working Group's modifications/actions/responses are summarized in Table 6.

Table 5. Responses to four items on the professional consultation survey.

	Number (%)				
General Questions: Overall Guideline Assessment	Lowest Quality (1)	(2)	(3)	(4)	Highest Quality (5)
1. Rate the overall quality of the guideline report.	0	0	6	38	25
	Strongly Disagree (1)	(2)	(3)	(4)	Strongly Agree

					(5)
2. I would make use of this guideline in my professional decisions.	1	0	7	31	30
3. I would recommend this guideline for use in practice*.	0	2	7	27	32
4. What are the barriers or enablers to the implementation of this guideline report?	The barriers listed in the professional consultation feedback include the pre-exercise assessment and how it would be funded, how one would access it, what would it include, who would conduct it and transportation to and from it. Other barriers include the lack of exercise programs with experience with cancer patients, the lack of exercise specialists, the lack of practitioner knowledge and comfort prescribing exercise, the time constraint in the clinical setting to discuss, the difficulty of getting patients who don't normally exercise to exercise, family and patient compliance, and the lack of a specific exercises and examples in the guideline. Enablers listed included that the guideline will encourage clinicians to talk to patients about maintaining a normal active life despite undergoing treatment or after treatment and encourage facilities to have dedicated time for those starting out in programs. The conclusions make sense and recommendations appear simple and provide a place to start by showing patients that exercise is not harmful. The guideline also allows recommendations for health care professionals to refer to for consistency in messaging to patients. The guideline may be promoted as part of rehabilitative recovery phase of treatment program.				

*One blank

Table 6. Modifications/actions/responses regarding main written comments from professional consultants.

Main written comments	Modifications, actions, or responses
1. Type of studies these types of research studies are based on the recommendations by ACSM that some PA is better than none and that a control group without PA is somewhat unethical at this stage of our understanding.	The comparison that the Working Group used was usual care. Indeed, a control group with no exercise allowed would not be good.
2. Define things better –resistance exercise	Resistance exercise is defined in the preamble to the recommendations.
3. The recommendations for a 'moderate amount' of exercise is ambiguous, when 'amount' refers to volume which includes intensity AND duration AND frequency. I would suggest that 'amount' be rephrased to intensity and that volume refers to the recommendations of min/wk. I believe the many will underestimate the quantity of 'moderate amount'. Refer to specific and clear RPE scale ratings in definition of intensity in summary and guideline (in addition to "x over baseline"). The RPE intensity scale seems to be the most easily understood and preferred intensity scale for patients and healthcare professionals to	The Working Group feels that this guideline is to inform health professionals that they should send their patients to exercise. It is then up to the exercise specialist to best inform/prescribe exercise to the patient. The Working Group added *(See Recommendation 3)* to Recommendations 1 and 2 to help quantify moderate amount immediately. The Working Group feels that intensity is explained in the preamble. There is information about RPE scales that can be found in: http://www.alcoa.ca/e/cancer_project/pdf/alcoa_exercis

	use and explain. Include a sample RPE scale for clarity and reference in the summary or appendix.	e_manual.pdf
4.	They will often ask exactly what they should be doing and how hard they should be pushing themselves. It may be of benefit to provide some recommendations or examples of acceptable exercise routines in the document, e.g. running or cycling at a certain % of maximum heart rate for age, or some other method that most patients could understand and use	The Working Group realizes that more guidance would be preferable but that the data did not supply enough information to be more exact. The patient's personal preferences and fitness levels will also play a role in their exercise routines. The Working Group will add an example of RPE so that people can better understand the effort needed to improve QoL.
5.	Explain group/supervised better and provide a reference on how to write or organize an exercise regimen	Unfortunately, the evidence did not provide much information on which type of group might be better than another. Paktakia [15] found that programs that improved QoL all were gym-based and under the supervision of a physiotherapist. Using a physiotherapist might result in regular monitoring, program adherence, support and encouragement but its costs. Using a gym can provide social interaction but can cost and can be intimidating. The Working Group will add the following link to the discussion that provides a guide for developing an exercise program for older adults living with cancer. http://www.alcoa.ca/e/cancer_project/pdf/alcoa_exercise_manual.pdf
6.	Further guidance for different levels of patients: debilitated versus those with increased fitness levels. Recommendations may indicate a need of 'a discussion with the treating physician (oncologist)'. A stage 1 patient is very different from a stage 4 and a blanket approach is not appropriate. The question of whether or not there are specific adaptations that are likely required at different stages/treatments of cancer is not well addressed.	The Working Group feels that this guideline is to inform health professionals that they should send their patients to exercise. It is then up to the exercise specialist to best inform/prescribe exercise to the patient. The Working Group feels that the physical issues that may occur are addressed in the ACSM guidelines in Appendix 8.
7.	More information on assessment (e.g. stress test, physiotherapy consult) and some recommendation about who to lead assessment. Safety concerns have been a primary concern for primary care providers and other healthcare professionals. Outline the specific pre-screening assessment recommendations, including CPET validated screening tool and a summary of ACSM suggested assessments provided in the full report. Refer to an appendix for ACSM guideline for more details information of site-specific medical assessments.	The Working Group feels this issue is met in the ACSM guidelines in Appendix 7. To ensure people are aware of that information we will make reference to the ACSM guideline in the preamble and discussion. As well, the Working Group will add a reference to a pre-exercise assessment paper in the discussion.

8.	Ongoing research into survival is important. I would suggest that the authors consider adding one additional question/section about priorities for future researchers interested in the topic of exercise in cancer patients.	The Working Group will add that research into survival and exercise is a priority into the discussion.
9.	Add list of established programs in Ontario	There is not a list of programs available. But the Working Group noted that it's important for people to find a place with certified exercise specialists.
10.	In the write up for QoL and muscular fitness, reference to/description of the guidelines in these areas was not made although in Table 1 it does indicate that there are guidelines for these.	The Working Group will add the data from the guidelines into the correct outcome areas.
11.	Is there ANY study showing the exercises ARE NOT GOOD?	No studies were found that showed exercise was harmful.

Abbreviations: ACSM: American College of Sports Medicine Roundtable on Exercise Guideline for Cancer Survivors; CPET: cardiopulmonary exercise testing; PA: physical activity; QoL: quality of life; RPE: rate of perceived exertion

CONCLUSION

The final guideline recommendations contained in Section 2 and summarized in Section 1 reflect the integration of feedback obtained through the external review processes with the document as drafted by the GDG Working Group and approved by the GDG Expert Panel and the PEBC RAP.

Appendix 1. Members of the Exercise for People with Cancer Guideline Development Group.

Expert Panel Members

Members	Affiliation	Conflict of interest
Roanne Segal*	Medical Oncologist Medical Lead, Breast Disease Site Head Survivorship Program The Ottawa Hospital	None
Esther Green*	Provincial Head, Nursing and Psychosocial Oncology Cancer Care Ontario	None
Caroline Zwaal*	Health Research Methodologist McMaster University	None
Jennifer Tomasone*	Exercise Psychologist McMaster University	None
Teresa Petrella*	Medical Oncologist Chair NCIC Melanoma Clinical Trials Group Sunnybrook Hospital	None
Andrew Loblaw*	Radiation Oncologist Scientist, Evaluative Clinical Sciences, Odette Cancer Research Program Sunnybrook Hospital	None
Caryl Russell	Director UW Fitness University of Waterloo	None
Oren Cheifetz	Physiotherapist Hematology/Oncology Program, CanWell Program Hamilton Health Sciences	None
Paul Oh	Medical Director Toronto Rehab–Cardiac Rehab Program University Health Network	None
Sara McEwen	Scientist St. John's Rehab Research Program Sunnybrook Research Institute	None
Chris Booth	Medical Oncologist Canada Research Chair in Population Cancer Care Cancer Centre of Southeastern Ontario	Yes: Study Co-chair for NCIC CTG C021
Jennifer Brunet	Assistant Professor School of Human Kinetics University of Ottawa	None
Susanna Cheng	Medical Oncologist Sunnybrook Hospital	None
Marie-Hélène Rivard	Patient Representative Ottawa, Ontario	None

***Working Group Member**

Report Approval Panel Members

Members	Affiliation	Conflict of interest
Melissa Brouwers	Director Program in Evidence-based Care	None
Donna Maziak	Surgeon Ottawa Hospital	None
Marko Siminovic	Surgeon Juravinski Cancer Centre	None

Appendix 2. List of Abbreviations and Measures.

Abbreviation/Measure	Definition
6MWT	**6-Minute walk test:** simple standardized measure of the distance walked during a defined period of time which assesses the submaximal level of functional capacity
95% CI	**95% Confidence interval:** estimated range of values which is likely to include an unknown population parameter, the estimated range being calculated from a given set of sample data
Active treatment	Treatment directed immediately to the cure of the disease or injury
Cohen's d	An effect size used to indicate the standardized difference between 2 means; uses the version of the standard deviation in which it is divided by N
CPET	**Cardiopulmonary exercise testing:** a noninvasive, objective method of assessing integrated response of heart, lungs, and musculoskeletal system to incremental exercise
EORTC QLQ-C30	**European Organisation for Research and Treatment of Cancer Quality of Life-C30:** an integrated system for assessing the health-related QoL of cancer patients participating in international clinical trials
FACT-B	**Functional Assessment of Cancer Therapy-Breast Cancer:** questionnaire used to measure the QoL of breast cancer patients undergoing treatment
FACT-B+4	**Functional Assessment of Cancer Therapy-Breast Cancer:** FACT-B with questions added to assess lymphedema
% HR_{max}; (Intensity measure)	**Percentage of maximum heart rate:** a way to measure the intensity level of exercise that a person is doing.
Hedges' g	The difference between means divided by the standard deviation; uses the version of the standard deviation in which it is divided by N–1
Heterogeneity	Any kind of variability among studies in a systematic review
HSCT	**Hematopoietic stem cell transplantation:** an infusion of a product (i.e., bone marrow, peripheral blood stem cell, cord blood, etc.)
METs (Intensity measure)	**Metabolic equivalent of task:** physiological measure expressing the energy cost of physical activities. one MET is equal to the amount of oxygen consumed while sitting at rest equal to 3.5 mL O_2 per kg body weight x min (O_2/kg/min)
NSCLC	**Non-small cell lung cancer**
Post treatment	Relating to, typical of, or occurring in the period following treatment
QoL	**Quality of life:** assessment of the perceived quality of a patient's daily life or their ability to enjoy normal life activities and general wellbeing.
HRQoL	**Health-related quality of life:** assessment of how the individual's wellbeing may be affected over time by a disease, disability, or disorder

RCT	**Randomized controlled trial**
SF-36	**Short Form Health Survey:** an instrument used to assess multidimensional health-related QoL, which measures eight health-related parameters: physical function, social function, physical role, emotional role, mental health, energy, pain, and general health perceptions
SMD	**Standardized mean difference:** a summary statistic in meta-analysis used to express the size of the intervention effect in each study relative to the variability observed in that study
UC	**Usual care:** definition has not been standardized; it can include the routine care received by patients for prevention or treatment of diseases
VO_{2max}	**Maximal oxygen consumption:** maximal oxygen uptake or the maximum volume of oxygen that can be used in one minute during maximal or exhaustive exercise
VO_{2peak}	**Peak oxygen consumption:** oxygen uptake at the maximal level of tolerated exercise
WMD	**Weighted mean difference:** difference between the intervention group and the control group across studies where the results of some of the studies make a greater contribution to the average than others

Appendix 3. Literature Search Strategy.

SYSTEMATIC REVIEWS	
MEDLINE	**EMBASE**
1. exercise.mp. or Exercise/ 2. cancer.mp. or Neoplasms/ 3. 1 and 2 4. (comment or letter or editorial or note or erratum or short survey or news or newspaper article or patient education handout or case report or historical article).pt. 5. 3 not 4 6. exp meta-analysis/ 7. (metaanal: or meta-anal: or metanal: or quantitative overview? or quantitative synthes#s).tw. 8. (systematic review? or systematic overview?).ti,tw. 9. 6 or 7 or 8 10. 5 and 9 11. limit 10 to yr="2005 -Current"	1. meta analysis/ 2. (meta-anal: or metaaanal: or metanal:).tw. 3. (systematic: review? or systematic: overview?).tw. 4. letter.pt. 5. book.pt. 6. editorial.pt. 7. note.pt. 8. exercise.mp. 9. cancer.mp. 10. neoplasm?.mp. 11. or/1-3 12. conference abstract.pt. 13. or/4-7,12 14. 11 not 13 15. 9 or 10 16. 8 and 15 17. 16 and 14 18. limit 17 to (human and english language and exclude medline journals)

RANDOMIZED CONTROLLED TRIALS	
MEDLINE	**EMBASE**
1. exercise.mp. or Exercise/ 2. neoplasms.mp. or Neoplasms/ 3. 1 and 2 4. randomized controlled trial.pt. 5. controlled clinical trial.pt. 6. randomized.ab. 7. 4 or 5 or 6 8. limit 7 to english language 9. limit 8 to yr="2011 -Current"	1. exercise.mp. or Exercise/ 2. neoplasms.mp. or Neoplasms/ 3. 1 and 2 4. ("randomized controlled trial" or "clinical trial" or placebo or trial or random$).mp. 5. randomized.ab. 6. 4 or 5 7. limit 6 to (human and english language) 8. limit 7 to yr="2011 -Current" 9. limit 8 exclude medline journals

Appendix 4. AGREE II scores for included guidelines.

Domain	ACSM	KCE	CSEP
Scope and Purpose	72%	94%	100%
Stakeholder Involvement	50%	58%	94%
Rigour of Domain	52%	81%	98%
Clarity and Presentation	75%	69%	78%
Applicability	31%	4%	46%
Editorial Independence	42%	46%	96%

Abbreviations: ACSM: American College of Sports Medicine Roundtable on Exercise Guideline for Cancer Survivors; CSEP: Canadian Society for Exercise Physiology Canadian Physical Activity Guidelines Clinical Practice Guideline Development Report; KCE: Belgium Health Care Knowledge Centre Report 185C – Supportive Treatment for Cancer Part 1: Exercise Treatment.

Appendix 5. AMSTAR results for included systematic reviews.

AMSTAR question	Systematic review																
	Gardner 2014	Cramer 2014	Cavalheri 2013	van Haren 2011	Strasser 2013	Focht 2013	Steins Bisschop 2012	Mishra 2012 Active	Mishra 2012 Post	Keogh 2012	Fong 2012	Baumann 2012	Pastakia 2011	McMillan 2011	Jones 2011	Duijts 2011	Ferrer 2011
1. Was an a priori design provided?	No	Yes	Yes	No	No	No	No	Yes	Yes	No	No	No	No	No	No	No	No
2. Was there duplicate study selection and data extraction?	Yes	Yes	Yes	Yes	Yes and no	Yes	Yes	Yes	Yes	No	Yes	Yes and no	Yes and no	Yes and no	Yes	Yes and no	Yes and no
3. Was a comprehensive literature search performed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Yes	No	Yes	No	No	No	No	Yes	Yes	Yes	No	No	No	No	No	No	Yes
5. Was a list of studies (included and excluded) provided?	No	Yes	Yes	No	Yes	No	No	Yes	Yes	No	No	No	No	No	No	No	No
6. Were the characteristics of the included studies provided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Was the scientific quality of the included studies assessed and documented?	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes and no	No
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No
9. Were the methods used to combine the findings of studies appropriate?	Yes	Yes	Yes	Yes	Yes	Can't Answer	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Was the likelihood of publication bias assessed?	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	No	Yes	No	Yes	Yes	Yes
11. Was the conflict of interest included?	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes

Appendix 6. Risk of bias results for included randomized controlled trials.

Trial	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other	Comment
Winters-Stone et al., 2015	Unclear	Unclear	High	Unclear	High	Low	Single blinded	Loss of follow-up; no info on pre-PA
Cormie et al., 2015	Unclear	Low	High	Unclear	Low	Low	Single blinded	No info on pre-PA; no follow-up
Porserud et al., 2014	Low	Low	High	Low	Unclear	Low	Single blinded	Lots of drop-outs; small sample size
Oechsle et al., 2014	Unclear	Unclear	High	High	Low	Low	-	Small sample size
Galvao et al., 2014	Low	Unclear	High	High	Low	Low	-	Control group received PA recommendations
Brocki et al., 2014	Low	Low	High	Low	Low	Low	-	Loss to follow-up
Bourke et al., 2014	Low	Unclear	High	Low	Low	Low	Single blinded	
Backman et al., 2014	Unclear	Unclear	High	High	Low	High		All self reported data
Arbane et al, 2014	Low	Low	High	High	Low	Low		
Santa Mina et al, 2013	Low	Low	High	High	Low	Low	Low power	
Rogers et al., 2013	Low	Low	High	High	High	low	Pilot	Small sample size
Mitgaard et al., 2013	Low	Unclear	High	Low	High	Low	Single blinded	High attrition
Lonbro et al, 2013	Unclear	Unclear	High	Low	Low	Low		Control group some attrition
Courneya et al., 2013	Low	Low	High	High	Low	Low		
Cormie et al., 2013	Low	Low	High	Unclear	Low	Low		Small sample size
Cormie et al., 2013	Low	Low	High	Unclear	Low	Low		Small sample size
Broderick et al., 2013	Low	Unclear	High	Low	Low			Small sample size
Andersen et al, 2013	Low	Unclear	High	High	Low	Low		
Stigt et al., 2013	Unclear	Unclear	High	Unclear	High	Low	Low power	Lots of dropouts; no info on pre-PA; increase in pain
Samuel et al., 2013	Low	High	High	High	High	High	-	No info on pre-PA, no adherence measure
Pinto et al., 2013	Unclear	Unclear	High	Low	High	Low	-	Personnel blinded for allocation
Hayes et al., 2013	Low	Unclear	High	Low	Low	Low	Exercise group: 25% did not increase exercise	Personnel blinded for allocation/ UC group increased PA same amount as IG; no pre-PA
Ergun et al., 2013	Low	Unclear	High	Low	Low	Low	Small sample size	No info on pre-PA; no adherence measure
Yeo et al., 2012	Unclear	Unclear	Unclear	Unclear	Low	Low	-	No info on randomization; not ITT; no info on pre-PA, no adherence measure
Schmidt et al., 2012	Unclear	Unclear	Unclear	Unclear	Low	High	Small sample size	UC=gymnastics; small n, no adherence measure
Saarto et al., 2012	Low	Low	High	High	Low	Low	-	Both groups increased exercise the same amount
Anderson et al., 2012	Low	Low	High	Unclear	Unclear	Low	-	Single blinded
Arbane et al., 2011	Low	Low	High	Low	Low	Low	-	Some loss to follow-up; no adherence

Abbreviations: IG: intervention group; ITT: Intention to treat; PA: physical activity; UC: usual care

Appendix 7. Pre-exercise Medical Assessments and Exercise Testing from the American College of Sport Medicine

	Breast	Prostate	Colon	Adult hematologic (no HSCT)	Adult HSCT	Gynecologic
General medical assessments recommended before exercise	Recommend evaluation for peripheral neuropathies and musculoskeletal morbidities secondary to treatment regardless of time since treatment. If there has been hormonal therapy, recommend evaluation of fracture risk. Individuals with known metastatic disease to the bone will require evaluation to discern what is safe before starting exercise. Individuals with known cardiac conditions (secondary to cancer or not) require medical assessment of the safety of exercise before starting. There is always a risk that metastases to the bone or cardiotoxicity secondary to cancer treatments will be undetected. This risk will vary widely across the population of survivors. Fitness professionals may want to consults with the patients' medical team to discern this likelihood. However, requiring medical assessment for metastatic disease and cardiotoxicity for all survivors before exercise is not recommended because this would create an unnecessary barrier to obtaining the well-established health benefits of exercise for the majority of survivors for whom metastasis and cardiotoxicity are unlikely to occur.					
Cancer site-specific medical assessments recommended before starting an exercise program	Recommend evaluation for arm/shoulder morbidity before upper body exercise.	Evaluation of muscle strength and wasting.	Patient should be evaluated as having established consistent and proactive infection prevention behaviors for an existing ostomy before engaging in exercise training more vigorous than a walking program.	None	None	Morbidly obese patients may require additional medical assessment for the safety of activity beyond cancer-specific risk. Recommend evaluation for lower extremity lymphedema before vigorous aerobic exercise or resistance training.
Exercise testing recommended	No exercise testing required before walking, flexibility or resistance training. Follow ACSM guidelines for exercise testing before moderate to vigorous aerobic training. One-repetition maximum testing has been demonstrated to be safe in breast cancer survivors with and at risk for lymphedema.					
Exercise testing mode and intensity considerations	As per outcome of medical assessments and following ACSM guidelines for exercise testing.					
Contraindications to exercise testing and reasons to stop exercise testing	Follow ACSM guidelines for exercise testing.					

Abbreviations: ACSM: American College of Sports Medicine; HSCT: hematopoietic stem cell transplantation

Appendix 8. American College of Sports Medicine person-specific exercise modification.

	Breast	Prostate	Colon	Adult hematologic (no HSCT)	Adult HSCT	Gynecologic
Objectives of exercise prescription	1. To regain and improve physical function, aerobic capacity, strength and flexibility 2. To improve body image and QoL 3. To improve body composition 4. To improve cardiorespiratory, endocrine, neurological, muscular, cognitive and psychosocial outcomes 5. Potentially to reduce or delay recurrence or a second primary cancer 6. To improve the ability to physically and psychologically with stand the ongoing anxiety regarding recurrence to a second primary cancer 7. To reduce, attenuate and prevent long-term and late effects of cancer treatment 8. To improve the physiologic and psychological ability to withstand any current or future cancer treatments These goals will vary according to where the survivor is in the continuum of cancer experience					
General contradictions for starting an exercise program common across all cancer sites	Allow adequate time to heal after surgery. The number of weeks required for surgical recovery may be as high as 8. Do not exercise individuals who are experiencing extreme fatigue, anemia or ataxia. Follow ACSM guideline for exercise prescription concerning cardiovascular and pulmonary contradictions for starting an exercise program. However, the potential for an adverse cardiopulmonary event might be higher among cancer survivors than age-matched comparisons given the toxicity of radiotherapy and chemotherapy and long-term/late effects of cancer surgery.					
Cancer-specific contradictions for starting an exercise program	Women with immediate arm or shoulder problems secondary to breast cancer treatment should seek medical care to resolve those issues before exercise training with upper body.	None	Physician permission recommended for patients with ostomy before participation in contact sports (risk of blow) and weight training (risk of hernia).	None	None	Women with swelling or inflammation in the abdomen, groin, or lower extremity should seek medical care to resolve these issues before exercise training with the lower body.
Cancer-specific reasons for stopping an exercise program.	Changes in arm/shoulder symptoms or swelling should result in reductions or avoidance of upper body exercise until after appropriate medical evaluation and treatment resolves the issue.	None	Hernia, ostomy-related systemic infection	None	None	Changes in swelling or inflammation of the abdomen groin, or lower extremities should result in reduction or avoidance of lower body exercise until after appropriate medical evaluation and treatment that resolves the issue.
General injury risk issues in common across cancer sites	Patients with bone metastases may need to alter their exercise program concerning intensity, duration and mode given increased risk for skeletal fractures, infraction risk is higher for patients who are currently undergoing chemotherapy or radiation treatment or have compromised immune function after treatment. Care should be taken to reduce infection risk in fitness centres frequented by cancer survivors. Exercise tolerance of patients currently in treatment and immediately after treatment may vary from exercise session to exercise session about exercise tolerance, depending on their treatment schedule. Individuals with known metastatic disease to the bone with require modifications and increased supervision to avoid fractures. Individuals with cardiac conditions (secondary to cancer or not) will require modification and may require increased supervision for safety.					
Cancer-specific risk of injury and emergency procedures	The arms/shoulders should be exercised but proactive injury prevention approaches are encouraged, given the high incidence of arm/shoulder morbidity in breast cancer survivors. Women with lymphedema should wear a well-fitting compression garment during exercise. Be aware of risk for fracture among those treated with hormonal therapy, a diagnosis of osteoporosis or bony metastases.	Be aware of risk for fracture among patients treated with ADT, a diagnosis of osteoporosis or boy metastases	Advisable to avoid excessive intra-abdominal pressures for patients with an ostomy.	Multiple myeloma patients should be treated as if they have osteoporosis	None	The lower body should be exercises but proactive injury prevention approaches are encouraged, given the potential for lower extremity swelling or inflammation in this population. Women with lymphedema should wear a well-fitting compression garment during exercise. Be aware of risk for fracture among those treated with hormonal therapies, with diagnosed osteoporosis or with bony metastases.

Abbreviations: ACSM: American College of Sports Medicine; ADT: androgen deprivation therapy; HSCT: hematopoietic stem cell transplantation; QoL: quality of life

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