Ontario Health
Cancer Care Ontario

**Guideline 19-5 Version 2**

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

# 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 was reviewed in 2024 and ENDORSED by the Expert Panel on Exercise for People with Cancer. (See Section 6: Document Assessment and Review for details)**

**Guideline 19-5 Version 2 is comprised of 6 sections. You can access the summary and full report here:**

**https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/201**



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**PUBLICATIONS RELATED TO THIS REPORT**

A clinical practice guideline article and a meeting report have been published in Current Oncology (http://www.current-oncology.com)

- Segal R, Zwaal C, Green E, Tomasone, JR, Loblaw A, Petrella T, and the Exercise for People with Cancer Guideline Development Group. Exercise for people with cancer: a clinical practice guideline. Current Oncology, v. 24, n. 1, p. 40-46, Feb. 2017. ISSN 1718-7729.
- Tomasone JR, Zwaal C, Kim GM, Yuen D, Sussman J, Segal R et al. Moving guidelines into action: a report from Cancer Care Ontario's event Let's Get Moving: Exercise and Rehabilitation for Cancer Patients. Current Oncology, v. 24, n. 1, p. e65-e74, Feb. 2017. ISSN 1718-7729.

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### Guideline Document History

| GUIDELINE VERSION | SYSTEMATIC REVIEW | | PUBLICATIONS | NOTES and KEY CHANGES |
|---|---|---|---|---|
| | Search Dates | Data | | |
| Original version June 30, 2015 | 2000 to 2014 | Full Report | Peer review publication. Web publication. | N.A. |
| Current Version 2 July 11, 2024 | 2023 to 2024 | New data found in Section 6: Document Assessment and Review | Updated web publication | 2015 recommendations are **ENDORSED** with minor additions |

**Guideline 19-5: Section 1**

# Exercise for People with Cancer: Recommendations Summary

**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 people living with cancer at different points in the cancer journey.

**TARGET POPULATION**

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

**INTENDED USERS**

Oncologists, qualified exercise professionals, 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, elastic resistance bands or own body weight 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, their adherence to recommendations and other health behaviours. 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. The most important thing is to avoid inactivity.

**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.

   **Added in 2024:** *Qualifying statement:* This recommendation also applies to advanced cancer and palliative care settings. (See Section 6 for details.)

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.

   **Added in 2024:** *Qualifying statement:* This also applies to prehabilitation/pretreatment exercise. (See Section 6 for details.)

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 for the general population. 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.

   **Added/Edited in 2024:** The American College of Sports Medicine has released more detailed information with exercise recommendations for specific cancer populations, other side effects and symptoms as well as an implementation guide which can be viewed at the following links:

   **Full Guideline**: https://journals.lww.com/acsm-msse/fulltext/2019/11000/exercise_guidelines_for_cancer_survivors_.23.aspx

   **Quick Visual Abstract**: https://www.acsm.org/blog-detail/acsm-certified-blog/2019/11/25/acsm-guidelines-exercise-cancer-download

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, including fracture risk.
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

*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**

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

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

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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, elastic resistance bands or their own body weight 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, their adherence to recommendations and other health behaviours. 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, 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.**

   **Added in 2024: *Qualifying statement*: This recommendation also applies to advanced cancer and palliative care settings. (See Section 6 for details.)**

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.**

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   - **150 minutes of moderate-intensity aerobic exercise spread over three to five days and resistance training at least two days per week;**
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**Quick Visual Abstract: https://www.acsm.org/blog-detail/acsm-certified-blog/2019/11/25/acsm-guidelines-exercise-cancer-download**

***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, weightlifting, 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 (3-6 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.cancercareontario.ca/sites/ccocancercare/files/assets/CCOPEBCDARP.pdf?redirect=true


## 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.

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*

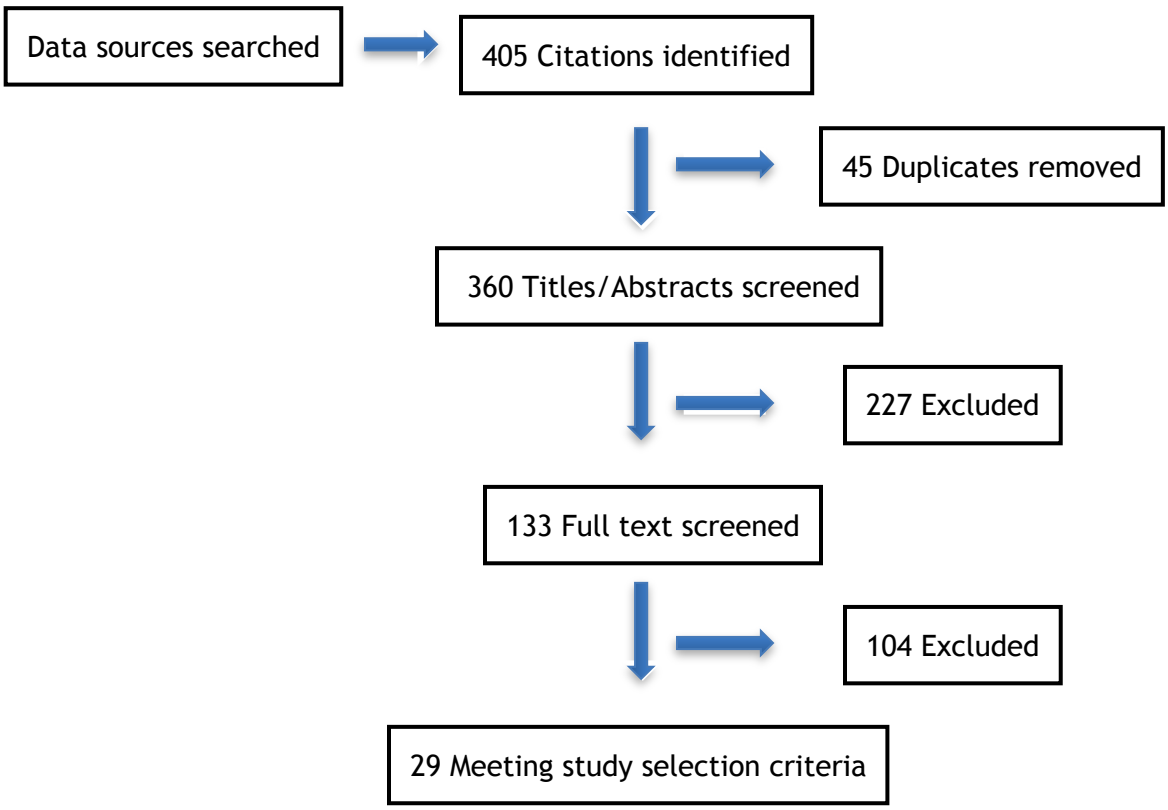

**Table 1. Sources selected for inclusion.**

| Question (exercise compared with usual care) | Number of sources that were included |
|---|---|
| Does exercise improve domains of QoL? | 1 guideline<br>14 systematic reviews<br>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<br>8 systematic reviews<br>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<br>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<br>6 systematic reviews<br>9 RCTs |
| What delivery models are appropriate for patients with different types or stages of cancer? | 1 guideline<br>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 ($\beta = -0.26$, $p<0.01$).

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]**<br><br>*Active treatment* | 10 studies;<br>565 prostate cancer patients with ADT<br>RCTs and pre-post studies | Various exercise interventions | • 5 RCTs and 4 UCTs included QoL measures<br>• 4 studies found significant or clinically meaningful benefits on QoL with exercise training, 5 studies observed no effect<br>• 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]**<br><br>*Post treatment* | 3 studies;<br>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<br><br>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<br><br>All 3 studies used different treadmill test protocols |
| **Cavalheri, 2013 [9]**<br><br>*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<br><br>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)<br><br>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<br>• 3 different types of exercise<br>• Small number of patients<br>• Different exercise regimens<br>• Assessed at different times |
| **van Haren, 2013 [21]**<br><br>*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]**<br><br>*Active and post treatment* | 9 studies; 752 cancer patients | Resistance training | Upper limb muscle strength:<br>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:<br>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]**<br><br>*Active and post treatment* | 15 studies; 1077 cancer patients | Resistance exercise | QoL: Cohen's *d*=0.25; range -0.72 to 1.14<br><br>Muscular strength: Cohen's *d*=0.86; range 0.11-2.45<br><br>Muscular endurance: Cohen's *d*=1.88; range 0.66-2.90 | |
| **Carayol, 2013 [4]**<br><br>*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<br><br>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]**<br><br>*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<br>Adverse events occurred in only 1% of CPET | 6 adverse events but only 55% of studies mentioned adverse events |
| **Mishra, 2012 [18]**<br><br>*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]**<br><br>*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 | |

| Study | Population, diagnosis | Interventions | Main findings | Comments |
|---|---|---|---|---|
| | 2 studies; 110 breast cancer patients | 6-mo follow-up | HRQoL: SMD=0.14, 95% CI -0.24 to 0.51, p=0.47; $I^2$=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]**<br><br>*Active and post treatment* | 12 studies; 498 cancer patients<br><br>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<br><br>Studies used EORTC-C30 and SF-36 | For overall QoL:<br>• Grade A recommendation for group-based exercise, resistance training<br>• Grade B recommendation for aerobic training<br>For HRQoL:<br>• "B" recommendations for group-based and resistance plus aerobic training<br>• "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<br>• Grade B recommendations were given when supported by at least one level 2 study<br><br>Grade C recommendations were given when supported by any non-RCT, level 3-5 studies |
| **Fong, 2012 [13]**<br><br>*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<br>Leg press (kg): SMD=19, 95% CI 9 to 28, p<0.01; $I^2$=71%, p=0.03 | |
| **Baumann, 2012 [8]**<br><br>*Active and post treatment* | 21 studies;<br>2118 prostate cancer patients | Physical activities or exercise interventions | Supervised exercise is more effective than non-supervised exercise<br>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.<br>Only 7 studies evaluated resistance or aerobic training programs; other pelvic floor/sphincter training |

| Study | Population, diagnosis | Interventions | Main findings | Comments |
|---|---|---|---|---|
| **Pastakia, 2011 [19]**<br><br>*Active and post treatment* | 9 studies;<br>breast cancer patients | Only RCTs with positive results<br>4 trials used FACT-B measures<br>Implemented between 5 wk to 6 mo | Summarized the interventions used<br>Mode: all trials included a warm up and cool down with an element of flexibility in the program<br>• 4 used only aerobic<br>• 1 used repeated limb movements with a chair<br>• 2 used a combination of aerobic and strengthening<br>• 1 used only strength<br>• All that used strengthening focused on low weights and high reps<br>Duration: range 14-60 min<br>• 4 used 60-min session<br>• 4 progressed from 14-35 min<br>• 1 did not report<br>Frequency:<br>• 7: 3×/week<br>• 1: 2×/week<br>• 1: 3×/week during 3 cycles of CT<br>Intensity:<br>• 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<br>Delivery and location:<br>all programs were gym-based and under supervision of physiotherapist | Developed recommendations for an exercise program |
| **McMillan, 2011 [16]**<br><br>*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]** | 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 | |

| Study | Population, diagnosis | Interventions | Main findings | Comments |
|---|---|---|---|---|
| *Active and post treatment* | 2 studies; 363 cancer patients | During treatment | $VO_{2peak}$: WMD=1.21, 95% CI 0.50 to 1.92, p=0.0008; $I^2$=0%, p=0.48 | |
| **Duijts, 2011 [6]**<br><br>*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]**<br><br>*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%<br><br>Weighted least-squares multiple regression, >26 weeks intervention + 4 METs<br>All intervention groups: Cohen's *d*=0.22, 95% CI 0.17 to 0.28<br>High-quality studies: Cohen's *d*= 0.16, 95% CI 0.010 to 0.22<br><br>>26 week intervention +8 METs<br>All interventions groups: Cohen's *d*=1.46, 95% CI 0.90 to 2.03<br>High-quality studies: Cohen's *d*=1.40, 95% CI 0.50 to 2.29<br><br>Intervention efficacy increased when the exercise was supervised (ß=−0.26, p <0.01) | • Included RCTs and pre-test comparison<br>• 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]**<br><br>*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.<br><br>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<br>Exercise: 87.5 (SD=14.3); 92.2 (SD=11.7); 93.3 (SD=9.0)<br>Control: 89.7 (SD=15.3); 82.4 (SD=20.1); 86.7 (SD=20.7)<br>Difference between groups at 6 mo: p<0.01<br>Difference between groups at 12 mo: p<0.01<br><br>**Quadriceps strength (leg press 1RM, kg)** score at baseline, 6 and 12 mo<br>Exercise: 121.3 (SD=33.5); 137.5 (SD=44.3); 142.4 (SD=52.2)<br>Control: 119.9 (SD=30.3); 121.8 (SD=33.4); 120.8 (SD=30.6)<br>Difference between groups at 6 mo: p=0.03<br>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)<br>• Median attendance to supervised classes was 84% in the resistance group. |
| **Cormie, 2015 [23]**<br><br>*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<br>Exercise: 54.1 (SD=7.9); 56.0 (SD=6.3)<br>Usual care: 53.1 (SD=10.0); 51.8 (SD=9.6)<br>Difference between groups: p=0.022<br><br>**Aerobic capacity ($VO_{2peak}$, mL/kg/min)** at baseline and 3 mo<br>Exercise: 22.1 (SD=3.5); 22.7 (SD=3.8)<br>Usual care: 23.2 (SD=3.4); 22.7 (SD=3.6) | |

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| | | | The usual care group was offered the program after the study was completed. | | | Difference between groups: p=0.004<br><br>**Quadriceps strength (leg press 1RM, kg)** score at baseline and 3 mo<br>Exercise: 134.3 (SD=50.0); 157.9 (SD=52.9)<br>Usual care: 143.6 (SD=52.4); 141.7 (SD=9.6)<br>Difference between groups: p<0.001 | |
| **Porserud, 2014 [38]**<br><br>*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.<br><br>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<br>Exercise: 5.6 (SD=10.0); 2.4 (SD=5.6)<br>Usual care: 2.1 (SD=16.0); 0.4 (8.1)<br>Difference between groups after training: p=1.00<br>Difference between groups at 1 year: p=0.67<br><br>**Aerobic capacity (6MWT)**<br>Increase from baseline to 12 wks and 12 wks to 1 year<br>Exercise: 112.9 (SD=40.1); 23.8 (SD=8.2)<br>Usual care: 62.8 (SD=26.3); -19.2 (SD=15.3)<br>Difference between groups after training: p=0.013<br>Difference between groups at 1 year: p=0.010 | • Small sample size<br>• Many dropouts<br>• Exercise group attended 76% (SD=67-95) of group exercise sessions and took daily walks 87% (SD=56-100) of the days |

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| **Oechsle, 2014 [24]**<br><br>*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<br>Exercise: 50<br>Usual care: 50<br>Between-group differences: p=0.66 | • No comparison for muscle strength<br>• Small sample size<br>• Significant difference for physical Function al QoL |
| **Galvao, 2014 [39]**<br><br>*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.<br><br>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<br>Exercise: 50.3 (SD=9.6); 51.6 (SD=6.6); 51.2 (SD= 7.5)<br>Control: 47.4 (SD=10.4); 47.1 (SD=9.5); 48.7 (SD=9.5)<br>Between-group difference at 6 mo: p=0.025<br>Between-group difference at 12 mo: p=0.649<br><br>**Aerobic capacity** (400 m walk time in seconds) at baseline, 6 mo and 12 mo<br>Exercise: 288.0 (SD=7.6); 269.4 (SD=8.4); 270.4 (SD= 7.3)<br>Control: 276.5 (SD=7.6); 279.4 (SD=8.4); 274.1 (SD=7.3)<br>Between-group difference at 6 mo: p=0.029<br>Between-group difference at 12 mo: p=0.028<br><br>**Quadriceps strength** (leg extension in kg) at baseline, 6 mo and 12 mo | • Physical activity recommendations given to the control group (should do over 150 minutes of moderate activity per week) |

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| | | | | | | Exercise: 50.7 (SD=3.0); 59.3 (SD=3.0); 56.6 (SD=2.8)<br>Control: 51.0 (SD=2.9); 49.9 (SD=2.9); 50.2 (SD=2.8)<br>Between group difference at 6 mo: p<0.001<br>Between group difference at 12 mo: p=0.011 | |
| **Brocki, 2014 [40]**<br><br>*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.<br><br>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<br>Exercise: 45.67; 4.4; 5.33<br>Control: 44.88; 5.4; 9.6<br>Between-group difference at 4 mo: p=0.99<br>Between-group difference at 1 year: p=0.27<br><br>**Aerobic capacity (6MWT)** at baseline, 4 mo change and 1 year change score<br>Exercise: 427m; 61m; 65 m<br>Control: 407m; 55m; 60m<br>Between-group difference at 4 mo: p=0.57<br>Between-group difference at 1 year: p=0.93 | • 43% the control group regularly exercised at home or joined an exercise program<br>• 43% of the exercise group reported exercising at home at least 2x weekly<br>• Supervised only 1/week<br>• Lost in follow-up: 43% of exercise group and 13% of control group |

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| **Bourke, 2014 [25]**<br><br>*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.<br>12 wk: mean difference: 8.9 points; 95% CI 3.7 to 14.2; adjusted p=0.001<br>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<br>• 82% of the prescribed independent exercise sessions over the first 12 wk. |
| **Backman, 2014 [26]**<br><br>*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.<br><br>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<br>Exercise: 64.4 (SD=17.7); 59.1 (SD=18.2)<br>Usual care: 62.9 (SD=19.1); 56.7 (SD=24.3)<br>No significant difference between groups over time points, p=0.881 | • 91% adherence average during intervention period<br>• 74% completed exercise intervention<br>• 34% reached the goal of 10,000 steps every week<br>• EORTC QLQ –BR23 found a significant difference of p=0.045 between groups. |

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| **Arbane, 2014 [27]**<br><br>*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.<br><br>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<br>No significant differences between groups from baseline to 4 wks after surgery.<br><br>**Quadriceps strength** (kg force)<br>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<br>• Did an airflow obstruction sub analysis and found a significant difference between groups for QoL: p=0.01 |
| **Santa Mina, 2013 [29]**<br><br>*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).<br><br>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<br>Aerobic: 123.9 (SE=3.2); 124.2 (SE=3.2)<br>Resistance: 119.3 (SE=3.6); 117.4 (SE=4.1)<br>Difference between groups: p=0.935<br><br>**QoL (PORPUS)** Baseline and 6 mo scores<br>Aerobic: 67.3 (SE=2.0); 65.8 (SE=2.1)<br>Resistance: 62.2 (SE=2.0); 62.3 (SE=2.2)<br>Difference between groups: p=0.625<br><br>**Aerobic capacity ($VO_{2peak}$;** mL/kg/min) Baseline and 6 mo scores<br>Aerobic: 25.1 (SE=1.8); 27.9 (SE=2.0)<br>Resistance: 28.4 (SE=1.6); 30.5 (SE=1.6) | • Aerobic group attended 16.4% of booster sessions; 27 did not attend any.<br>• Resistance group attended 5.5% of sessions; 22 did not attend any.<br>• Log books not completed effectively<br>• No control group<br>• Small sample size |

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| | | | | | | Difference between group: p=0.565<br><br>**Grip strength (kg)** Baseline and 6 mo scores<br>Aerobic: 63.9 (SE=2.6); 64.5 (SE=2.7)<br>Resistance: 69.6 (SE=2.0); 68.9 (SE=2.3)<br>Difference between group: p=0.865 | |
| **Rogers, 2013 [31]**<br><br>*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<br>Exercise: 73.8 (SD=14.8); 66.8 (SD=18.4); 70.6 (SD=18.2)<br>Control: 90.4 (SD=10.8); 76.0 (SD=16.0); 84.6 (SD=13.8)<br>Difference between groups: Baseline to 6 wks: 7.4 (SD=14.2), d=0.52<br>Baseline to 12 wks: 6.6 (SD=16.9), d=0.39 | • Very small sample size |
| **Midtgaard, 2013 [7]**<br><br>*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.<br><br>Goal was to have participants exercise at least 3 hours/week.<br><br>Heath Evaluation Group had three, health evaluation session that included feedback following fitness testing and | 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<br>Exercise: 67.21 (95% CI 62.70 to 71.56); 84.53 (95% CI 80.27to 88.36)<br>Control: 67.16 (95% CI 62.65to 71.52); 81.17 (95% CI 76.78 to 85.19)<br>Treatment Effect Ratio= 1.04 (95% CI 0.95 to 1.14), p=0.276<br><br>**Aerobic capacity ($VO_{2peak}$;** mL/min) Baseline and 12 mo mean.<br>Exercise: 1.97 (95% CI 1.89 to 2.05); 2.34 (95% CI 2.24 to 2.44) | • Adherence to the weekly-supervised exercise training sessions was 66.6%.<br>• Heart rate during supervised exercise sessions was 77 ± 7% of the measured heart rate maximum.<br>• Significant improvements in physical activity in the control group<br>• High attrition rate; 24% in control group; 32% in exercise group. |

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| | | | education on health benefits of regular exercise. | | | Control: 1.99 (95% CI 1.91 to 2.08); 2.28 (95% CI 2.18 to 2.38) Treatment Effect Ratio= 1.04 (95% CI=1.00 to 1.07), p= 0.032<br><br>**Quadriceps strength (Leg Press kg)**<br>Baseline and 12 month mean<br>Exercise: 81.76 (95% CI 76.34 to 87.57); 109.68 (95% CI 101.98 to 117.97)<br>Control: 84.54 (95% CI 78.89 to 90.60); 92.84 (95% CI 86.38 to 99.77)<br>Treatment Effect Ratio: 1.22 (95% CI 1.15 to 1.30), p <0.001 | |
| **Lønbro, 2013 [42]**<br><br>*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:<br>Early exercise group:<br>19 (SD=14)<br>Delayed exercise group:<br>6 (SD=12)<br>Between group difference<br>p<0.05 | • Early: 17 of 19 patients returned their training logs. Based on these patients the mean training adherence rate was 91%.<br>• Delayed: 10 of 15 patients returned their training logs. Based on these patients the mean training adherence rate was 98%. |
| **Courneya, 2013 [33]**<br><br>*Active treatment* | 96 aerobic exercise intervention (STAN); 101 high dose aerobic exercise intervention (HIGH); | Adult women with breast cancer during chemotherapy | STAN: 75 min vigorous aerobic exercise per week<br>HIGH: 150 minutes vigorous aerobic exercise per week<br>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 | No serious adverse events were related to exercise. | **QoL (SF-36-general health),**<br>Linear mixed –model analyses<br>COMB vs. STAN Mean: −0.7, (95% CI −2.6 to 1.1); p=0.44;<br>HIGH vs. STAN Mean: +0.6, (95% CI −1.2 to 2.5); p=0.50;<br>HIGH vs. COMB Mean: +1.4, (95% CI −0.5 to 3.2); p=0 .14. | • Higher doses of exercise were achievable and safe. |

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| | 104 combined aerobic and resistance exercise intervention (COMB) | | | Aerobic activity: 3x/wk, Strength training: 3x/wk | | **Aerobic capacity ($VO_{2peak}$; mL/kg/min)**<br>Linear mixed –model analyses<br>COMB vs. STAN Mean: −0.2, (95% CI −1.2 to 0.8); p=0.70;<br>HIGH vs. STAN Mean: +0.9, (95% CI −0.1 to 1.9); p=0.08;<br>HIGH vs. COMB Mean: +1.1, (95% CI 0.1 to 2.1); p=0 .03.<br><br>**Quadriceps strength (Leg Press -kg)**<br>Linear mixed –model analyses<br>COMB vs. STAN Mean: +6.0, (95% CI 1.4 to 10.7); p=0.01;<br>HIGH vs. STAN Mean: +0.0, (95% CI −4.6 to 4.6); p=0.99;<br>HIGH vs. COMB Mean: -6.0, (95% CI -10.7 to -1.4); p=0.01. | |
| **Cormie, 2013 [5]**<br><br>*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.<br><br>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<br>High-load Exercise: 2.9 (SE=1.7)<br>Low-load Exercise: 6.6 (SE=1.6)<br>Usual care: 1.7 (SE=1.7)<br><br>No significant difference between groups, p=0.195.<br><br>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<br>• Significant difference between groups for SF-36 -physical function |

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| **Cormie, 2013 [44]**<br><br>*Post treatment* | 10 exercise intervention;<br>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.<br><br>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<br>Exercise: 44.1 (SD=10.1); 42.6 (SD=12.9)<br>Usual care: 43.5 (SD=7.2); 43.9 (SD=11.4)<br>No significant difference between groups, p=0.475 | • High attendance (83%) and compliance rates (93%) |
| **Broderick, 2013 [45]**<br><br>*Post treatment* | 23 exercise intervention;<br>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.<br><br>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<br>Exercise: 86.2 (SD=14.8); 90.0 (SD= 12.5); 92.1 (SD=14.0)<br>Usual care: 91.6 (SD=7.5); 95.4 (SD=11.3); 93.3 (SD=19.0)<br>No significant difference between groups at time points, p=0.94, p=0.37<br><br>**Aerobic capacity ($VO_{2peak}$;** mL/kg/min) at baseline, 2 and 3 mo, respectively<br>Exercise: 19.7; 24.1; 22.8<br>Usual care: 19.1; 20.2; 20.4<br>No significant difference between groups at time points, p=0.14, p=0.61 | • 60.9% attended > 70% of group exercise classes<br>• 78.3 % met home exercise program guidelines<br>• Participants had very low fitness levels at start |
| **Andersen, 2013 [34]**<br><br>*Active treatment* | 106 exercise intervention;<br>107 wait-list control | Adults with cancer receiving chemotherapy | 4.5 hours high intensity training (cardio and heavy resistance)<br>1.5 hours body awareness<br>2 hours relaxation<br>1 hour massage<br><br>Usual care group was offered an exercise | 9 hours/wk for 6 wks | Adverse events were not reported. | **QoL (FACT-G score)**<br>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.<br>• Adherence was 75% |

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| | | | program after study completion. | | | | |
| **Stigt, 2013** [28]<br><br>*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)**<br>No significant difference between exercise and usual care groups<br><br>**Aerobic capacity (6MWT)**<br>Exercise: 35m increase<br>Usual care: 59m decrease<br>Significant difference between groups, p=0.024 | • High dropout rate<br>• Conclusion: waiting 3-4 mo may be better<br>• Increase in exercise tolerance caused more pain and physical limitations<br>• In exercise group, only 33% of patients on ACT completed the program, whereas 83% of patients not on ACT completed it |
| **Samuel, 2013** [30]<br><br>*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)**<br>Exercise: 11.73% increase<br>Usual care: 75.21% decrease<br>Significant difference between groups, p<0.001<br><br>**Aerobic capacity (6MWD)**<br>Exercise: 42m increase<br>Usual care: 96m decrease<br>Significant difference between groups, p<0.001 | • Adherence not measured |
| **Pinto, 2013** [41]<br><br>*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<br><br>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<br>End: 5×/wk for 12 wks | Adverse events were not reported. | **QoL (FACT-C score),** at baseline, 3, 6, and 12 mo, respectively<br>Exercise: 105.3; 111.3; 111.7; 110.7<br>Usual care: 105.3; 110.8; 108.7; 110.6<br>No significant difference.<br><br>**Aerobic capacity ($VO_{2peak}$;** mL/kg/min) at baseline, 3, 6, and 12 mo, respectively | • 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<br>• No real exercise program<br>• Primary outcome was increase in physical activity with an |

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| | | | Assessments at baseline, 3, 6, and 12 mo. | | | Exercise: 22.97; 27.65; 28.43; 27.06<br>Usual care: 22.97; 23.71; 24.36; 22.12<br>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]<br><br>*Active treatment* | 67 exercise group with face-to-face support;<br>67 exercise group with telephone support;<br>60 usual care | Adult women diagnosed with breast cancer 6 wk post-surgery | Individually tailored program<br>16 sessions (in person or via telephone) with exercise physiologist weekly then tapered to monthly<br><br>Wk 1-4: aerobic, low-to-moderate intensity, 20-30 min<br><br>Wk 5-8: aerobic with strength introduced, moderate intensity, 30-40 min<br><br>Wks 9-32: aerobic and strength, moderate to high intensity, ≥45 min<br><br>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<br>Exercise (face-to-face): +9.5 (95% CI 5.3 to 3.8)<br>Exercise (telephone): +13.5 (95% CI 10.0 to 17.0), p≤0.05<br>Usual care: +6.5 (95% CI 1.8 to 11.1)<br><br>Face to face and telephone group had clinically meaningful change over time.<br>Significant between-group differences in QoL between telephone group and usual care group (p≤0.05)<br><br>**Aerobic fitness (modified 3-min step test)** change in heart rate from baseline to 12 mo post-surgery<br>Exercise (face-to-face): -9.0 (95% CI -12.9 to -5.2), p≤0.05<br>Exercise (telephone): -6.3 (95%CI -10.2 to -2.4), p≤0.05<br>Usual care group: +2.7 (95% CI -3.0 to 8.4)<br><br>Face-to-face group had clinically meaningful change over time.<br>Significant differences were found between the face-to-face | • 88% of face-to-face group and 81% of telephone group completed scheduled sessions with exercise physiologist<br>• 25% in face-to-face and telephone groups did not meet intervention goal of increasing total physical activity between measures<br>• 66% of women in usual care group participated in ≥180 min of activity/wk and/or increased activity by 30 min/wk |

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

| Author | Sample size | Population, diagnosis | Intervention | Frequency and duration | Adverse events | Main findings | Comments |
|---|---|---|---|---|---|---|---|
| *Active treatment* | 79 completed study at final follow-up at 19 mo | periampullary cancer | Monthly diary and monthly phone call<br><br>Warm up, brisk walking, cool down:<br>Mo 1: 5, 10, 5 min<br>Mo 2: 5, 20, 5 min<br>Mo 3: 5, 25-30, 5 min<br><br>Low-to-moderate intensity. | | | Usual care: 44; 48<br><br>Significant difference between groups, p≤0.05 | |
| **Schmidt, 2012** [46]<br><br>*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)<br>Usual care group: weekly conventional gymnastics exercises, such as chair or floor exercises<br>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**<br>Exercise: 59 (SD=16.6); 67 (SD=19.9); 76 (SD=12.9); p<0.01<br>Usual care: 67 (SD=17.2); 75 (SD=18.0); 77 (SD=15.3); p<0.01<br><br>No significant difference between groups. | Usual care group in this study used conventional exercise gymnastics |
| **Saarto, 2012** [47]<br><br>*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)<br><br>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<br>Exercise: 4.2 (95% CI 1.9 to 6.6)<br>Usual care: 5.6 (95% CI 3.1 to 8.1)<br><br>No significant difference between groups, p=0.43 | • Adherence: 62% for supervised weekly training sessions<br>• 88% trained mean 3.2 hr/wk<br>• Median number of training sessions was 3.8/wk<br>• Very active usual care group; therefore, no |

| Author | Sample size | Population, diagnosis | Intervention | Frequency and duration | Adverse events | Main findings | Comments |
|---|---|---|---|---|---|---|---|
| | | | | | | **Aerobic capacity (2MWT; m),** difference from baseline to 12 mo<br>Exercise: -0.89 (95% CI -1.03 to -0.76)<br>Usual care: -0.72 (95% CI -0.85 to -0.58)<br><br>No significant difference between groups, p=0.15<br><br>For all participants, significant linear trend between higher physical activity (increase in METs/wk) and improved QoL, p=0.011 | difference between groups<br>• The exercise group increased physical activity by 3.10 MET-h/wk<br>• 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<br>• Not sensitive enough questionnaire (for patients not survivors) |
| **Eakin, 2012** [36]<br><br>*Active treatment* | 68 exercise intervention; 69 usual care | Women with invasive breast cancer | 16 calls with exercise physiologist of 15-30 min<br>0-2 mo: 1×/wk<br>2-4 mo: 1×/2 wk<br>4-8 mo: 1×/mo<br><br>Target:<br>45 min, moderate-to-vigorous aerobic activity + strength-based exercise at least 2×/wk;<br>Exercise workbook provided.<br><br>Assessments at baseline, 6 and 12 mo post-surgery. | 45 min<br>4×/wk<br>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<br><br>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<br>• Change from baseline to 12-mo post-surgery clinically meaningful in QoL and upper body function for exercise group only |
| **Anderson, 2012** [3] | 52 exercise intervention; 52 usual care | Adult women with stage I-III breast cancer | RESTORE: centre-based moderate tailored exercise program | 65 min<br>2×/wk for 12 mo | 39 adverse events; 7 serious, but only 2 events | **QoL (FACT-B score),** mean at baseline and 18 mo Exercise: 102.6 (SD=16.9); 115.8 (SD=1.6) | • Primarily examined exercise-induced lymphedema |

| Author | Sample size | Population, diagnosis | Intervention | Frequency and duration | Adverse events | Main findings | Comments |
|---|---|---|---|---|---|---|---|
| *Post treatment* | | | 0-3 mo: 2×/wk for 60 min; 20 min resistance training and 30 min walking<br><br>4-6 mo: option for home-based, 1×/wk at centre<br><br>7-12 mo: exercise at home or facility<br><br>Assessments at baseline, 6, 9, 12, 15, and 18 mo. | | were deemed study-related (pectoral muscle pain and stress fracture in foot). | Usual care: 103.7 (SD=22.1); 114.4 (SD=2.5)<br>No significant differences between groups, p=0.57<br><br>**Aerobic capacity: (6MWT; m),** mean at 18 mo<br>Exercise: 593.2 (SE=13.0)<br>Usual care: 558.9 (SE=11.8)<br><br>The exercise group walked significantly further, p=0.0098 | • 71.2% of participants completed all prescribed sessions (0-97%)<br>• 61% of participants attended more than 75%<br>• 13% attended <50% of sessions |
| **Arbane, 2011** [37]<br><br>*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<br><br>Walking and strength training adapted to patient.<br><br>60%-80% of maximal heart rate. | 5-10 min to start then adapted to individual<br><br>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<br>Exercise: 6.5 (95% CI –7.7 to 20.7)<br>Usual care: 2.2 (95% CI -5.2 to 9.6)<br><br>No significant difference over time or between groups<br><br>**Aerobic fitness (6MWT; m),** mean at pre, 5-day postoperative and 12-wk follow-up, respectively<br>Exercise: 466.6 (SD=102.1); 336.7 (SD=84.1); 480.2 (SD=110.0)<br>Usual care: 455.7 (SD=98.0); 308.7 (SD=124.8); 448.2 (SD=95.1)<br><br>Repeated measures analysis:<br>Overall: within-subjects time effect, p<0.001; group effect, p=0.47 | • No adherence information<br>• No clear intervention information after 5-day postoperative<br>• Some loss to follow-up<br>• 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 |
|---|---|---|---|---|---|---|---|
| | | | | | | From preoperative to 5 day post-op (paired t tests): between-subjects group time effect, p=0.89<br><br>**Quadriceps strength (magnetic stimulation of femoral nerve; kg),** mean at pre, 5-day postoperative and 12-wk follow-up, respectively<br>Exercise: 33.2 (SD=15.2); 37.6 (SD=27.1); 34.2 (SD=9.4)<br>Usual care: 29.1 (SD=10.9); 21.5 (SD=7.7); 26.4 (SD=9.7)<br><br>Repeated measures analysis: within-subjects time effect, p=0.70<br>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.<br>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.<br><br>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.<br>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.<br><br>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.<br><br>The Working Group will add a link to an existing exercise program for cancer patients in the discussion.<br>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 alternative forms of exercise such as yoga. | The Working Group recognizes that flexibility is important but the definition of exercise used in this guideline was 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.<br><br>"Finally, it is recommended that adults engage in flexibility activities 3-4 times per week.<br>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"?<br>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.<br><br>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 | 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.<br><br>The Working Group added *(See Recommendation 3)* to Recommendations 1 and 2 to help quantify moderate amount immediately.<br><br>The Working Group feels that intensity is explained in the preamble. There is information about RPE scales that can be |

| | | |
|---|---|---|
| | easily understood and preferred intensity scale for patients and healthcare professionals to use and explain. Include a sample RPE scale for clarity and reference in the summary or appendix. | found in: http://www.alcoa.ca/e/cancer_project/pdf/alcoa_exercise_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.<br><br>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.<br><br>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.<br><br>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.<br>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.<br><br>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.<br>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<br>Medical Lead, Breast Disease Site<br>Head Survivorship Program<br>The Ottawa Hospital | None |
| Esther Green* | Provincial Head, Nursing and Psychosocial Oncology<br>Cancer Care Ontario | None |
| Caroline Zwaal* | Health Research Methodologist<br>McMaster University | None |
| Jennifer Tomasone* | Exercise Psychologist<br>McMaster University | None |
| Teresa Petrella* | Medical Oncologist<br>Chair NCIC Melanoma Clinical Trials Group<br>Sunnybrook Hospital | None |
| Andrew Loblaw* | Radiation Oncologist<br>Scientist, Evaluative Clinical Sciences, Odette Cancer Research Program<br>Sunnybrook Hospital | None |
| Caryl Russell | Director UW Fitness<br>University of Waterloo | None |
| Oren Cheifetz | Physiotherapist<br>Hematology/Oncology Program, CanWell Program<br>Hamilton Health Sciences | None |
| Paul Oh | Medical Director<br>Toronto Rehab–Cardiac Rehab Program University Health Network | None |
| Sara McEwen | Scientist<br>St. John's Rehab Research Program<br>Sunnybrook Research Institute | None |
| Chris Booth | Medical Oncologist<br>Canada Research Chair in Population Cancer Care<br>Cancer Centre of Southeastern Ontario | Yes: Study Co-chair for NCIC CTG C021 |
| Jennifer Brunet | Assistant Professor<br>School of Human Kinetics<br>University of Ottawa | None |
| Susanna Cheng | Medical Oncologist<br>Sunnybrook Hospital | None |
| Marie-Hélène Rivard | Patient Representative<br>Ottawa, Ontario | None |

***Working Group Member**

**Report Approval Panel Members**

| Members | Affiliation | Conflict of interest |
|---|---|---|
| Melissa Brouwers | Director<br>Program in Evidence-based Care | None |
| Donna Maziak | Surgeon<br>Ottawa Hospital | None |
| Marko Siminovic | Surgeon<br>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/<br>2. cancer.mp. or Neoplasms/<br>3. 1 and 2<br>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.<br>5. 3 not 4<br>6. exp meta-analysis/<br>7. (metaanal: or meta-anal: or metanal: or quantitative overview? or quantitative synthes#s).tw.<br>8. (systematic review? or systematic overview?).ti,tw.<br>9. 6 or 7 or 8<br>10. 5 and 9<br>11. limit 10 to yr="2005 -Current" | 1. meta analysis/<br>2. (meta-anal: or metaaanal: or metanal:).tw.<br>3. (systematic: review? or systematic: overview?).tw.<br>4. letter.pt.<br>5. book.pt.<br>6. editorial.pt.<br>7. note.pt.<br>8. exercise.mp.<br>9. cancer.mp.<br>10. neoplasm?.mp.<br>11. or/1-3<br>12. conference abstract.pt.<br>13. or/4-7,12<br>14. 11 not 13<br>15. 9 or 10<br>16. 8 and 15<br>17. 16 and 14<br>18. limit 17 to (human and english language and exclude medline journals) |

| RANDOMIZED CONTROLLED TRIALS | |
|---|---|
| **MEDLINE** | **EMBASE** |
| 1. exercise.mp. or Exercise/<br>2. neoplasms.mp. or Neoplasms/<br>3. 1 and 2<br>4. randomized controlled trial.pt.<br>5. controlled clinical trial.pt.<br>6. randomized.ab.<br>7. 4 or 5 or 6<br>8. limit 7 to english language<br>9. limit 8 to yr="2011 -Current" | 1. exercise.mp. or Exercise/<br>2. neoplasms.mp. or Neoplasms/<br>3. 1 and 2<br>4. ("randomized controlled trial" or "clinical trial" or placebo or trial or random$).mp.<br>5. randomized.ab.<br>6. 4 or 5<br>7. limit 6 to (human and english language)<br>8. limit 7 to yr="2011 -Current"<br>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 Ans-wer | 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 consult 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<br>2. To improve body image and QoL<br>3. To improve body composition<br>4. To improve cardiorespiratory, endocrine, neurological, muscular, cognitive and psychosocial outcomes<br>5. Potentially to reduce or delay recurrence or a second primary cancer<br>6. To improve the ability to physically and psychologically with stand the ongoing anxiety regarding recurrence to a second primary cancer<br>7. To reduce, attenuate and prevent long-term and late effects of cancer treatment<br>8. To improve the physiologic and psychological ability to withstand any current or future cancer treatments<br>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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Ontario Health
Cancer Care Ontario

**Guideline 19-5: Section 6**

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

# Exercise for People with Cancer

### Document Assessment and Review

*K. Rossini, C. Zwaal, and the Expert Panel on Exercise for People with Cancer*

**The 2015 guideline recommendations are ENDORSED**

**This means that the recommendations are still current and relevant for decision making**

**OVERVIEW**

The original version of this guidance document was released by Cancer Care Ontario's Program in Evidence-based Care in 2015.

In December 2022, this document was assessed in accordance with the PEBC Document Assessment and Review Protocol and was determined to require a review. As part of the review, a PEBC methodologist (CZ) conducted an updated search of the literature. A clinical expert (KR) reviewed and interpreted the new eligible evidence and proposed the existing recommendations could be endorsed. The Expert Panel on Exercise for People with Cancer (Appendix 1) endorsed the recommendations found in Section 1 (Clinical Practice Guideline) in July 2024.

**DOCUMENT ASSESSMENT AND REVIEW RESULTS**

**Questions Considered**

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, VO2 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.

**Literature Search and New Evidence**

The new search (2017 to February 2024) yielded 7 practice guidelines. A search from 2023-February 2024 yielded 14 SRs and 14 RCTs. Brief results of these publications are shown in the Document Summary and Review Tool evidence tables below.

**Impact on the Guideline and Its Recommendations**

The new data support the existing recommendations. As well, new evidence has shown exercise to be safe with advanced disease and palliative care. Prehabilitation/pretreatment exercise is also recommended to prevent muscle loss and complications which may allow for patients to tolerate treatment better.

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# Document Review Tool

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| **Number and Title of Document under Review** | 19-5 Exercise for People with Cancer |
| **Original Report Date** | June 30, 2015 |
| **Date Assessed (by DSG or Clinical Program Chairs)** | March 22, 2022 |
| **Health Research Methodologist** | Caroline Zwaal |
| **Clinical Expert** | Kathleen Rossini PT |
| **Approval Date and Review Outcome (once completed)** | July 11, 2024<br>ENDORSE |

Original 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, VO2 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.

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

Study Selection Criteria:

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

Search Details:
EMBASE 2017 to February 26, 2024
MEDLINE 2017 to February 26, 2024
Limited to English only; systematic reviews and RCTs
Search strategy identical to that used for original 2015 guideline

Summary of new evidence:

Retrieval:
Systematic review/guideline/RCT search/: 2384 citations
Title and abstract review:
Guidelines: 106 relevant citations
Systematic reviews: 67 relevant citations
RCTs: 148 relevant citations
Full text review for only 2023 and 2024:
Guidelines: 9
Systematic reviews: 23 relevant
RCTs: 64 relevant
Included:
Guidelines: 7
Systematic reviews: 14
RCTs: 14
Excluded:
RCTs or systematic reviews of non-repetitive exercise regimens or no definitive aerobic or muscular component. Programs with only behavioural counselling or meditation were not included.

Details from the included trials are summarized in the tables below.

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| 1. Does any of the newly identified evidence contradict the current recommendations? (i.e., the current recommendations may cause harm or lead to unnecessary or improper treatment if followed) | No. |
| 2. Does the newly identified evidence support the existing recommendations? | Yes, and provides more clarity and definition. |
| 3. Do the current recommendations cover all relevant subjects addressed by the evidence? (i.e., no new recommendations are necessary) | Yes.<br>Note that: Exercise is also safe with advanced disease and palliative care, and prehabilitation exercises are also safe before surgery/treatment, prevent muscle loss and complications, and allow patients to tolerate treatment better. |
| **Review Outcome as recommended by the Clinical Expert** | ENDORSE |
| ***If outcome is UPDATE, are you aware of trials now underway (not yet published) that could affect the recommendations?*** | |
| **DSG/Expert Panel Commentary** | There is some literature to suggest that 90 minutes, rather than the standard 150 min, of moderate intensity aerobic exercise is sufficient for certain outcomes in the cancer population<br>Could still state 150 minutes of MVPA for overall health for people living with and beyond cancer, but this is an opportunity to also highlight the specific FITT prescriptions that are now available which suggests that people living with and beyond cancer can exercise 90 minutes of MVPA/week and alleviate cancer-related side effects which is an important message to get out. So even if people living with and beyond cancer don't achieve 150 minutes of MVPA, if they get 90 minutes, they are still reaping benefits which isn't emphasized as much in the document<br>Recommendation of at least 90 minutes a week - refer to the Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable noted below. Recommendation of 150 minutes per week it's overwhelming for most patients<br>Some emphasis around 'avoiding inactivity' after a cancer diagnosis should be stressed. In addition, specific ACSM FITT guidelines would be helpful given that there are prescriptions for common cancer treatment side effects, this should be outlined in text even though there is an infographic referenced. I think some explanation around exercising during and after cancer treatment improves fatigue, anxiety, depression, physical function, quality of life and does not exacerbate lymphedema should be included in the recommendations along with the specific FITT prescriptions for each side effect (e.g., moderate- |

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| | intensity aerobic exercise at least 3 times per week, for at least 30 minutes and resistance exercise at least 2 times per week, doing at least 2 sets of 8 to 15 repetitions, using a weight or resistance that is at least 60% of a person's one-repetition maximum<br><br>For recommendation #6, the benefits extend beyond aerobic, muscular, and QoL benefits in light of the ACSM guidelines so fatigue, physical function, anxiety, depression, etc should be added. Mentioning that there is moderate evidence for bone health and sleep would also be good to include.<br><br>There is a subsection in the Discussion titled "Safety". It may be worth specifically noting fracture risk and weight bearing status as a safety consideration. From clinical experience, this is an area that is often overlooked in exercise prescription but can have significant impact to patient safety, particularly for patients with advanced disease and boney metastases or lytic lesions from Multiple Myeloma. I understand that this guideline isn't intended to provide specifics on how to progress a client's exercise program in the background of them being at high risk of fracture or having protected weight-bearing status, but I do believe that it is important at minimum to include this terminology so that health care providers are aware and vigilant of this.<br><br>There is a subsection in the Discussion titled "Cancer Type". It seems to focus on solid tumour cancer types (breast, prostate, lung cancer etc). It may be worth mentioning something about the hematological cancers and specific exercises considerations for this population (low blood counts, particularly low hemoglobin and platelets, and risk of bleeding). The hematological cancers (leukemia, myeloma, lymphoma) are making up an increasing population of primary and secondary cancers and there are specific rehabilitation and survivorship needs for this group. |

**Evidence Tables**

**Summary of Relevant Guidelines**

| Citation (ref) | Search dates | Recommendations |
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| Rock 2022 (1)<br><br>Survivors<br><br>ACS | From January 1, 2018, through November 7, 2020, for the physical activity/exercise searches<br><br>Studies of physical activity published during or after 2018, after systematic literature reviews of the American College of Sports Medicine (ACSM) roundtable report on physical activity, sedentary behavior, and cancer prevention and control and the 2018 "Exercise guidelines for cancer survivors: consensus statement from international multidisciplinary roundtable" were published. | General recommendations for cancer survivors:<br>• Nutritional assessment and counseling should begin as soon as possible after diagnosis, with the goal of preventing or resolving nutrient deficiencies, preserving muscle mass, and managing side effects of treatments that may adversely affect nutritional status.<br>• Physical activity assessment and counseling should begin as soon as possible after diagnosis, with the goal of helping patients prepare for treatments, tolerate and respond to treatments, and manage some cancer related symptoms and treatment-related side effects.<br><br>Recommendations to improve long-term health and increase the likelihood of survival:<br>• Avoid obesity and maintain or increase muscle mass through diet and physical activity.<br>• Engage in regular physical activity, with consideration of type of cancer, patient health, treatment modalities, and symptoms and side effects.<br>• Follow a healthy eating pattern that meets nutrient needs and is consistent with recommendations to prevent chronic disease.<br>• Follow the general advice of the American Cancer Society Guideline for Diet and Physical Activity for Cancer Prevention to reduce risk of a new cancer<br><br>American Cancer Society Guideline on Nutrition and Physical Activity for Cancer Prevention Recommendations for Individuals<br><br>2. Be physically active.<br>• Adults should engage in 150-300 min of moderate-intensity physical activity per week (or 75-150 min of vigorous-intensity physical activity); striving to meet or exceed the upper limit of 300 min is ideal.<br>• Children and adolescents should engage in at least one hour of moderate intensity or vigorous-intensity activity each day.<br>• Move more and sit less. |
| Ligibel, 2022 (2)<br><br>Active Cancer Treatment<br><br>ASCO | Jan 2000-May 2021<br><br>42 SR<br>23 RCT | Question 1: Does exercise during cancer treatment safely improve outcomes related to QoL, treatment toxicity, or cancer control?<br><br>Recommendation 1.1.<br>Oncology providers should recommend aerobic and resistance exercise during active treatment with curative intent to mitigate side effects of cancer treatment (Type: evidence-based; benefits outweigh harms; Evidence quality: moderate to low; Strength of recommendation: strong).<br>Note: Exercise interventions during active treatment reduce fatigue; preserve cardiorespiratory fitness, physical functioning, and strength; and in some populations, improve QoL and reduce anxiety and depression. In addition, exercise interventions during treatment have low risk of adverse events. |

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| | | Evidence was not sufficient to recommend for or against exercise during treatment to improve cancer control outcomes (recurrence or survival) or treatment completion rates.<br><br>Recommendation 1.2.<br>Oncology providers may recommend preoperative exercise for patients undergoing surgery for lung cancer to reduce length of hospital stay and postoperative complications (Type: evidence based, benefits outweigh harms; Evidence quality: low; Strength of recommendation: weak). |
| Campbell, 2022 (3)<br><br>Bone Metastases<br><br>Follow ACSM guidelines<br><br>JCO Oncology Practice | Up to July 16, 2020<br><br>The International Bone Metastases Exercise Working Group (IBMEWG) developed best practice recommendations on the basis of published research, clinical experience, and expert opinion using (1) modified Delphi survey, (2) systematic review, (3) cross-sectional survey to physicians and nurse practitioners, (4) inperson meeting, and (5) stakeholder engagement<br><br>17 RCTs | Regular exercise has the potential to maintain or improve physical function and health-related quality of life in people with bone metastases, and the perceived risk of skeletal complication should be weighed against the potential health benefits.<br>1. Before exercise testing or training, perform a risk assessment to inform the likelihood of a skeletal complication from exercise.<br>2. Consultation with the medical team is strongly encouraged before an exercise professional provides structured exercise for a person with bone metastases, to obtain key medical information and establish bidirectional communication for initial assessment and exercise training throughout care.<br>3. Exercise professionals best suited to prescribe exercise to people with bone metastases are physical therapists and clinical exercise physiologists (or equivalent), who have additional cancer exercise training and appropriate experience in working with people with a cancer diagnosis.<br>4. Professional judgment should be used to consider if exercise testing at baseline and follow-up is necessary by weighing the risks and benefits of including the test or if the testing protocols may need to be modified.<br>5. Exercise prescription should follow the standard exercise recommendations as outlined by the International Exercise Guidelines for Cancer Survivors, with greater emphasis on postural alignment, controlled movement, and proper technique, as well as consideration given to the location and presentation of the bone lesion(s). Formal monitoring of exercise response and adjustment of exercise prescription should be ongoing. |
| Neuzillet 2021 (4)<br><br>Digestive Cancer<br><br>French intergroup | Up to January 2019<br><br>Based on published guidelines, recent literature review and expert opinions. Recommendations are graded according to the level of evidence | Physical Activity Recommendations<br><br>Pre-treatment recommendations<br>• Assessment of physical condition (expert agreement):<br>  ○ Clinical: PS and VAS of fatigue (threshold ≥4) at diagnosis then at each consultation; PA level, resting HR and BP at diagnosis and then every 3–6months.<br>  ○ Elements that can impact the practice of PA: symptomatic tumour locations, comorbidities, poly-medication, motivation, fatigue, pain, psychosocial environment<br><br>PA in the perioperative setting<br>• Education and information of the patient about the benefits of PA (reduction of fatigue and the risk of postoperative complications), from the consultation for disease announcement (expert agreement).<br>• Early postoperative mobilisation by a physiotherapist (expert agreement).<br>• Limit sedentary behaviours (sitting or bedtime) and encourage regular PA (progressive implementation and taking into account postoperative limitations), by combining aerobic and resistance exercises, before and after surgery (expert agreement). |

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| | | During (Chemo) Radiotherapy<br>• Education and information of the patient about the benefits of PA during treatment (reduction of fatigue and increase of physical fitness), from the consultation for disease announcement (expert agreement).<br>• Limit sedentary behaviour (sitting or bedtime) and encourage regular PA (progressive implementation and taking into account the side effects and constraints of radiotherapy), combining aerobic and resistance exercises (expert agreement).<br><br>During Systemic Treatment<br>• Patient education and information on the benefits of PA during and after treatments (reduction of fatigue, improvement of HRQoL, and of physical fitness, potential effect on survival), from the consultation for disease announcement (expert agreement).<br>• Limit sedentary behaviours (sitting or bedtime) and encourage regular PA (progressive implementation and taking into account the side effects of treatments), at least partially supervised, combining aerobic and resistance exercises (expert agreement).<br>• Refer whenever possible to an APA professional for supervision, in particular for patients with barriers to PA or at risk: sarcopenia, comorbidities, metastatic disease, intense fatigue and or significant and recent drop in PA level, negative beliefs and fears about PA (expert agreement).<br><br>Advanced Palliative Phase<br>None (but options)<br><br>After Treatments<br>• Colorectal cancer (expert agreement) – Encourage and support behavioural changes in order to increase PA level, gradually, maintained over time and regularly. PA practice includes spontaneous activities of daily living and structured voluntary exercise sessions, supervised or not. – Objective of 150min of moderate aerobic PA distributed throughout the week and two sessions per week of resistance exercises of large muscle groups (upper limbs, lower limbs and trunk) while respecting 1-2days of recovery between two sessions.<br>• All tumour locations (expert agreement) – Education and information of the patient on the benefits of PA after treatment (reduction of fatigue, improvement of HRQoL, and of physical fitness, potential effect on the risk of recurrence and survival), from the consultation for disease announcement. – Limit sedentary behaviours (sitting or bedtime) and encourage regular PA (progressive implementation and taking into account the after-effects of treatments), combining aerobic and resistance exercises. |
| Jeevanantham, 2021 (5)<br><br>Multiple myeloma | Up to August 2018<br><br>17 studies:<br>7 RCT<br>7 cohort<br>3 case studies<br><br>Consensus | 1. Physical therapy intervention for patients with multiple myeloma in an acute care setting should not be withheld only based on lower hemoglobin values. Decisions should be made based on complete presentation, vitals, and symptoms.<br>2. Well-monitored physical therapy intervention can be safely administered to patients with MM with lower hemoglobin levels (less than 8 g/dL) in consultation with a physician and while carefully monitoring vital signs and signs of adverse events prior to, during and post intervention<br>3. A well-monitored physical therapy intervention can be provided to patients with multiple myeloma who are receiving RBC transfusion by carefully monitoring vital signs, complete presentation of the |

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| | | patient, and signs of adverse events<br><br>Platelet counts<br>4. A well-monitored individualized physical therapy intervention may be provided in patients with platelet counts greater than 10,000/μL after consultation with a physician<br>a. When the platelet counts are less than 10,000/μL, essential ambulation with assistance/supervision, and gentle range of motion exercises in lying or sitting without strain may be performed if no signs of bleeding or no history of recent bleeding.<br>b. When the platelet counts are between 10,000 and 20,000/μL, gentle range of motion exercises, strength training exercises without resistance while lying, sitting or standing, and ambulation as tolerated may be performed if no signs of bleeding or no history of recent bleeding.<br>c. When the platelet counts are between 20,000 and 40,000/μL, light resistance exercises using elastic bands may be performed if no signs of bleeding or no history of recent bleeding.<br>d. When the platelet counts are greater than 40,000/μL, gentle aerobic exercises including stationary cycling may be performed if no signs of bleeding or no history of recent bleeding.<br>e. Physical therapists should educate patients about the risk of falls, risk of bleeding, signs of bleeding, caution against injury, importance of proper footwear and clothing and compliance to recommendations by health care professionals including assistance, supervision, and assistive devices<br>f. Physiotherapist should monitor for signs of bleeding such as epistaxis, gingival bleeding, bruising, petechiae, ecchymosis, sign of intracranial hemorrhage, gastrointestinal bleeding, prior to, during, and post physical therapy sessions especially for patients with platelet counts lower than10,000/μL.<br>Note: *Physical therapists must do the following when implementing the above recommendations: (1) discuss with physician, (2) assess risk of fall and ensure patient safety, (3) use their expertise and clinical judgment in determining the specificity and safety of the exercises.*<br>*For the purpose of this guideline the term "essential ambulation" refers to required walking for essential activities like activities of daily living (ADL).*<br><br>White blood cell count<br>5. Additional precautions should be considered when providing physical therapy intervention to patients with MM with lower WBC counts.<br>a. Patients with neutropenia or leukocytopenia should wear a face mask and wash hands thoroughly when ambulating in the hallway and/or crowded areas.<br>b. Physical therapy equipment should be properly sanitized before being used for patients with neutropenia or leukocytopenia.<br>c. For patients with neutropenia or leukocytopenia physical therapy sessions should preferably be provided in patient's room rather than therapy department to reduce the risk of infections.<br><br>Bony lesions<br>6. Physical therapists should consult with physicians regarding risk of fractures and weight bearing status and take appropriate precautions and adaptations using critical thinking skills and clinical judgement in prescribing exercises in patients with MM with bony lesions |

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| | | Exercise Recommendations before/during/after receiving medical treatment:<br><br>*Before Treatment (Action Statement 7):*<br>7. Clinicians may offer home-based/unsupervised aerobic exercise to patients with MM to increase cardiorespiratory fitness and physical activity levels during the ambulatory period before autologous high-dose stem cell transplant (HSCT) (*evidence quality: III; recommendation strength: grade C*).<br><br>*During Treatment (Action Statements 8-9):*<br>*8.* Clinicians may offer supervised mixed aerobic/strength training exercise in the inpatient or outpatient setting to patients with MM while undergoing chemotherapy/HSCT (*evidence quality: III; recommendation strength: grade C*).<br>a. Clinicians may offer generalized rehabilitation and/or aerobic/strength training exercise during treatment to increase functional mobility, physical activity, and/or physical performance after chemotherapy/HSCT (*evidence quality: III; recommendation strength: grade C*).<br>b. Clinicians may offer aerobic/strength training exercise during treatment to improve QoL and reduce fatigue after chemotherapy/HSCT (*evidence quality: III; recommendation strength: grade C*).<br>c. Clinicians may offer aerobic/strength training exercise during treatment to increase muscular strength after chemotherapy/HSCT (*evidence quality: IV; recommendation strength: grade C*).<br><br>Special Circumstance Statement:<br>d. Clinicians may offer supervised mixed aerobic/strength training exercise to patients with MM with fracture risk and/or skeletal issues (i.e., bone lesions) while undergoing chemotherapy/HSCT (*evidence quality: IV; recommendation strength: grade C*).<br><br>9. Clinicians may offer home-based (unsupervised) mixed aerobic/strength training to patients with MM undergoing chemotherapy/HSCT (*evidence quality: I; recommendation strength: grade B*)<br>a. Clinicians may offer mixed aerobic/strength training to improve nighttime sleep and decrease fatigue during chemotherapy/HSCT (*evidence quality: II; recommendation strength: grade B*).<br>b. Clinicians may offer mixed aerobic/strength training to increase or maintain aerobic capacity and physical activity during chemotherapy/HSCT (*evidence quality: I; recommendation strength: grade B*).<br>c. Clinicians may offer mixed aerobic/strength training to maintain lean body weight and muscle strength during chemotherapy/HSCT (*evidence quality: II; recommendation strength: grade B*).<br><br>Special Circumstance Statement:<br>d. Clinicians may offer mixed aerobic/strength training exercises to patients with MM receiving epoetin alfa to reduce anemia symptoms during chemotherapy/HSCT (*evidence quality: I; recommendation strength: Grade B*).<br><br>*After Treatment (Action Statement 10):*<br>*10.* Clinicians may offer supervised and/or unsupervised individualized strength and aerobic or strength training alone in the outpatient and/or home-based setting to multiple myeloma patients when they |

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| | | are medically stable after chemotherapy/HSCT (*evidence quality: II; recommendation strength: grade B*)<br>a. Clinicians may offer aerobic/strength training or strength training alone to increase QOL and decrease fatigue after chemotherapy/HSCT (*evidence quality: II; recommendation strength: grade B*).<br>b. Clinicians may offer aerobic/strength training exercise or strength training alone to increase physical activity and/or physical fitness after chemotherapy/HSCT (*evidence quality: II; recommendation strength: grade B*).<br>c. Clinicians may offer combined aerobic/strength exercise or strength training alone to increase functional ability after chemotherapy/HSCT (*evidence quality: II; recommendation strength: grade B*). |
| Rock, 2020 (6)<br><br>Cancer Prevention<br><br>ACS | The current ACS Diet and Physical Activity Guideline and recommendations provide an update to the 2012 ACS guideline and are based largely on the WCRF/AICR systematic reviews and Continuous Update Project reports, supplemented with evidence from systematic reviews and large pooled analyses that have been published since the most recent WCRF/AICR reports | 1. Achieve and maintain a healthy body weight throughout life.<br>• Keep body weight within the healthy range and avoid weight gain in adult life.<br><br>2. Be physically active.<br>• Adults should engage in 150-300 min of moderate-intensity physical activity per week, or 75-150 min of vigorous-intensity physical activity, or an equivalent combination; achieving or exceeding the upper limit of 300 min is optimal.<br>• Children and adolescents should engage in at least 1 hr of moderate- or vigorous-intensity activity each day.<br>• Limit sedentary behavior, such as sitting, lying down, and watching television, and other forms of screen-based entertainment. |
| Campbell, 2019 (7)<br><br>Cancer Survivors<br><br>ACSM | Up to June 2018<br><br>Update to 2010 ACSM guideline<br><br>Roundtable<br>Frequency, intensity, time and type (FITT)<br><br>4 studies addressing HRQoL | Based on the current literature, an effective exercise prescription that most consistently addresses health-related outcomes experienced due to a cancer diagnosis and cancer treatment includes:<br>• Moderate-intensity aerobic training at least three times per week, for at least 30 min, for at least 8 to 12 wk.<br>• The addition of resistance training to aerobic training, at least two times per week, using at least two sets of 8 to 15 repetitions at least 60% of one repetition maximum, appears to result in similar benefits.<br>• The fitness professional should be prepared to an create exercise program that meet their clients' needs.<br>• Special considerations and modifications to exercise programs have been adapted from the NCCN guidelines |

ACS: A Cancer Journal for Clinicians; ACSM: American College of Sports Medicine; ASCO: American Society of Clinical Oncology; NCCN: National Comprehensive Cancer Network; WCRF/AICR: the World Cancer Research Fund/American Institute for Cancer Research;

FITT: Frequency, Intensity, Time and Type; HR: Heart Rate; HRQoL: Health-related Quality of Life; HSCT: High-dose Stem Cell Transplant; MM: Multiple Myeloma; PA: Physical Activity; QoL: Quality of Life; RCT: Randomized Controlled Trial; SR: Systematic Review.

**Summary of Relevant Systematic Reviews**

| Citation | Search details | Inclusion criteria | Intervention/comparison | Results | Included studies |
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| Lu, 2024 (8)<br><br>Lung cancer<br><br>Various times<br><br>9 studies | April 2022<br><br>Embase, PubMed, Scopus, and MEDLINE<br><br>Keywords: lung cancer, exercise, physical activity, depression, quality of life, randomized controlled trial, and meta-analysis | RCTs, English, studies with adult participants (≥18 years), studies with a minimum of 4 weeks of exercise intervention, studies reporting outcomes of interest (depression and quality of life). | PA, walking, aerobic+ tai chi, multimodal, resistance, pulmonary rehabilitation, structured exercise program, qigong education and rehabilitation vs usual care. | Nine RCTs. The pooled SMD exercise interventions on quality of life was 0.61, indicating a statistically significant association between quality of life and exercise interventions ($p < 0.001$). | Bade 2021<br>Chen 2015<br>Cheung 2021<br>Mikkelsen 2022<br>Molassiotis 2015<br>Morano 2014<br>Quist 2020<br>Vanderbyl 2017<br>Sui 2020 |
| Yuan, 2023 (9)<br><br>Prostate cancer<br><br>Androgen deprivation therapy<br><br>4 studies | April 2022<br><br>Web of Science, Embase, PubMed, Cochrane Library, China National Knowledge Infrastructure (CNKI), Wanfang Databases, VIP Journals Database, and Chinese Biomedical Databases<br><br>Search terms included prostatic neoplasms, prostate neoplasm, prostate cancer, androgen deprivation therapy, exercise, physical activity, meta-analysis, and systematic review | SR/MA, Participants were diagnosed with PCa and underwent ADT, primary outcome measure was body composition. The secondary outcomes included mood, QoL, physical function, cardiometabolic changes, bone mineral density (BMD), and sexual function. | Resistance or aerobic exercise training vs usual care | Four SR/MA reported that exercise training could improve the QoL of patients<br><br>Disease-specific QoL in PCa patients undergoing ADT (SMD:0.43, 95% CI: 0.29-0.58, $I^2$=11%, p<0.00001)<br><br>Simple exercise training significantly improved patients' QoL (SMD:0.17, 95% CI: 0.00-0.34, $I^2$=0%, p=0.05) | Shao 2022<br>Teleni 2016<br>Ussing 2022<br>Yang 2017 |
| Wang, 2023 (10)<br><br>Network Meta-analysis<br><br>Breast cancer<br><br>Post treatment | April 2023<br><br>Electronic searches in PubMed, Cochrane Reviews, Cochrane CENTRAL, Web of Science, and ClinicalTrials.gov | (1) RCTs that recruited breast cancer survivors who had completed treatments, including surgery, chemotherapy, and/or radiation therapy, (2) RCTs that investigated the quantitative assessment of | 12 week intervention of either: aerobic exercise; strength exercise; aerobic exercise plus strength exercise; yoga; or control<br><br>QoL as measured by the Functional Assessment of | Network meta-analysis revealed that among breast cancer survivors, aerobic and strength training was the most effective type of 12-week exercise intervention in improving QoL (effect size: 1.31; 95% CI: 0.49 to 2.12) | Lin 2023<br>Soriano-Maldonado 2022<br>Kim 2020<br>Stan 2016<br>Rogers 2015<br>Cramer 2015<br>Baruth 2015 |

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| 9 studies | databases using the following keywords: ('breast cancer') AND ('quality of life' OR 'QoL') AND ('exercises' OR 'physical activity' OR 'yoga' OR 'aerobic') AND ('random' OR 'randomized' OR 'randomised') AND ('12 weeks' OR '3 months') | quality of life after exercise intervention, (3) the control group that received no intervention or regular care, and (4) trials that had available data on quality of life pre- and post-intervention at 12 weeks. | Cancer Therapy-Breast (FACT-B) or the International Breast Cancer Study Group Quality of Life or cancer specific QoL tool such as the EORTC-QoL | Aerobic activity had a borderline effect (effect size: 0.83; 95% CI: 0.03 to 1.63), while yoga and strength exercise showed no significant difference compared to the control group | Ergun 2013<br>Milne 2008 |
| Tsou, 2023 (11)<br><br>Prostate cancer<br><br>Receiving androgen deprivation therapy<br><br>11 studies | August 2021<br><br>PubMed, Embase, and Cochrane Library databases.<br>The following terms were used and combined using the Boolean search strategy: androgen deprivation therapy, androgen suppression therapy, prostate cancer, physical activity, and exercise. | (i) Clear inclusion and exclusion criteria for the patients, (ii) the exercise and exercise protocols, (iii) stage of prostate cancer, and (iv) definition and evaluation of postintervention cancer related fatigue and received ADT during the study period or ongoing biochemical castration due to previous ADT. | Most of the exercise included in the meta-analysis combined aerobic and resistance training.<br><br>Aerobic exercises consisted of walking or jogging on the treadmill, cycling, or rowing on an ergometer at moderate to high intensity, such that 55% to 85% of the maximum heart rate predicted by age was achieved.<br><br>Resistance training consisted of body weight or free-weight training | QoL improved significantly in the exercise group (SMD: 0.18, 95% CI: 0.04 to 0.33) (11 studies)<br><br>The weight of the 1RM leg press improved significantly in the exercise group (SMD: 0.73, 95% CI: 0.42 to 1.05) (6 studies)<br><br>The 1RM chest-press weight was significantly improved in the exercise group (SMD: 0.42, 95% CI: 0.17 to 0.67) (6 studies) | Bourke 2011<br>Buffart 2015<br>Cormie 2015<br>Culos-reed 2010<br>Dawson 2018<br>Galvao 2010<br>Hojan 2017<br>Ndjavera 2020<br>Nilsen 2015<br>0'Neill 2015<br>Segal 2003 |
| Trommer, 2023 (12)<br><br>Prostate and breast cancer<br><br>During Radiation Therapy alone<br><br>2 studies | October 2022<br><br>CENTRAL, MEDLINE (Ovid), Embase (Ovid), CINAHL, conference proceedings and trial registries | RCTs that enrolled people who were receiving RT without adjuvant systemic treatment for any type or stage of cancer | Aerobic and resistance exercises for one, only aerobic for the other | 2 studies showed that exercise may have little or no effect on QoL (positive SMD values signify better QoL; low certainty).<br>SMD: 0.40, 95% CI −0.26 to 1.05; 37 participants (QoL measured with WHOQOL-BREF)<br>SMD: 0.47, 95% CI −0.40 to 1.34; 21 participants (QoL measured with FACT-P) | Hwang 2008<br>Monga 2007 |

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| Toohey, 2023 (13)<br><br>Palliative care phase for people with advanced cancers<br><br>22 studies<br><br>lung (n=6), breast (n=3), prostate (n=2), multiple myeloma (n=1) and mixed cancer types (n=10) | April 2021<br><br>Cochrane Library, EMBASE, SPORTDiscus (via EBSCOhost), ProQuest Health and Medical Complete, ProQuest Nursing and Allied Health Source, Science Direct, Web of Science, CINAHL, Scopus and PubMed<br><br>Combinations of MeSH and free-text words for "palliative", "cancer", "physical activity" and "exercise" | Included female or male adult participants, diagnosed with any type of incurable cancer currently in the stable palliative care phase<br><br>RCTs designed to evaluate the effects of exercise interventions; compared exercise to either no exercise, a different mode of exercise; evaluated safety, feasibility and/or the effectiveness of exercise on health-related outcomes | Interventions comprised of aerobic (n=3), resistance (n=4), mixed-mode (n=14) and other exercise - yoga (n=1)<br><br>Frequency 3–7 days/week for 2 weeks to 6 months (2–4 days per week of resistance exercise and daily walking)<br><br>Duration 20–120 min per session (including 5–15-min warm-up and cool-down) | Compared with usual care, there were small to moderate effects (all $p<0.05$); in favour of exercise for QOL (SMD=0.27(95% CI=0.14, 0.39)), fatigue (SMD=0.30 (95% CI=0.13, 0.47)), aerobic fitness (SMD=0.30 (95% CI=0.12, 0.49)) and lower-body strength (SMD=0.48 (95% CI=0.12, 0.84)<br><br>no difference in the risk of a grade 2–4 adverse event between exercise and usual care (n=110 adverse events (exercise: n=66 events; usual care: n=44 events), RD= −0.01 (91% CI=−0.01, 0.02); p=0.24)<br><br>No significant subgroup effects of exercise mode, supervision, duration and cancer-type were observed | QoL -11 studies<br><br>Aerobic fitness - 15 studies<br>Upper body strength -7 studies<br>Lower body strength -10 studies<br><br>Can't access list |
| Tanriverdi, 2023 (14)<br><br>Palliative care<br><br>14 studies<br><br>5 -mixed cancer<br>4 -lung cancer<br>2 -spinal metastases<br>1 -GI cancer<br>1 -Metastatic BC<br>1 -Metastatic CRC | July 2021<br><br>Embase, PubMed, and Web of Science. The four key terms were used including exercise, cancer, palliative, and random* | Included: (a) RCTs; (b) original studies published in English; (c) participants aged 18 years and older diagnosed with cancer receiving palliative care; (d) exercise interventions (e.g., aerobic and/or strength training); and (e) studies that assessed the effect of exercise on exercise capacity, muscle strength (handgrip and quadriceps muscle), physical activity, disease specific health-related quality of life (HRQoL), physical functioning, and cancer-related symptoms (fatigue, pain, and dyspnea) | 4 -resistance exercise;<br>1 -walking exercise;<br>8 -combined aerobic and resistance;<br>1 -combined aerobic, resistance and balance exercise<br>12 -supervised<br>2 -unsupervised<br>length ranged from 2 - 12 weeks<br>frequency ranged from 2-5 times per week<br><br>Number of studies compared exercise to:<br>10-usual care;<br>1-manual touch; | Disease specific HRQoL was significantly different between the exercise group and control group, and this favored the exercise group (SMD: 0.23; 95% CI=0.02 to 0.43; $I^2$=45%; six studies)<br><br>Exercise capacity was significantly higher in the exercise group compared to the control group (SMD: 0.37; 95% CI=0.07 to 0.67; $I^2$=67%; nine studies) | Rutkowska 2021<br>Edbrooke 2019<br>Poort 2020<br>Quist 2020<br>Henke 2014<br>Zimmer 2018<br><br>Edbrooke 2019<br>Henke 2014<br>Oldervoll 2011<br>Quist 2020<br>Quist 2020<br>Schuler 2017<br>Schuler 2017<br>Yee 2019<br>Zimmer 2018 |

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| | | | 1-conventional physiotherapy;<br>1 -passive physical therapy;<br>1 -muscle relaxation | | |
| Sun, 2023 (15)<br><br>Breast cancer survivors<br><br>Post treatment<br><br>20 studies | April 2022<br><br>PubMed, Embase, Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO, SinoMed, CNKI, VIP, and WanFang databases<br><br>“breast cancer,” “breast neoplasm,” “breast cancer survivors,” “exercise,” “physical activity,” “resistance training,” “aerobic exercise,” “quality of life,” “depression,” and “anxiety.” | Randomized controlled trials of the effects of physical activity on QoL, anxiety, or depression in breast cancer survivors | Aerobic training (e.g., walking, Tai Chi Chuan) and/or resistance training or both together<br><br>Duration: range 1-12 months<br><br>Follow-up: 3 months-1 year | 20 studies in the meta-analysis<br><br>Compared to usual care, significant improvement on QoL (Hedges' g = 0.67; 95% CI 0.41–0.92) p<0.01 | Dieli-Conwright 2018<br>Do 2015<br>Dong 2019<br>Ergun 2013<br>Ergun 2013<br>Eyigor 2021<br>Galiano-Castillo 2016<br>Hagstrom 2016<br>Littman 2012<br>Luca 2016<br>Murtezani 2014<br>Ochi 2022<br>Rogers 2015<br>Shobeiri 2016<br>Sprod 2012<br>Strunk 2018 |
| Sun, 2023 (16)<br><br>Lung cancer<br><br>11 studies<br><br>Mind–body exercise (yoga, tai chi, qigong, etc.) | May 2023<br><br>PubMed, Web of Science, Cochrane Library, Embase, CNKI, CBM, WanFang Data, and VIP<br><br>(1) “Tai Chi” OR “Tai Chi Chuan” OR “Taiji” OR “Qigong” OR “Chi Kung” OR “Qi Gong” OR “Baduanjin” OR “Yijinjing” OR “Wuqinxi” OR “Yoga” OR “mind–body” OR “pilates”; (2) “Lung Neoplasm*” OR “Pulmonary Neoplasm*” | (1) Experimental group using different modalities of mind–body exercise as an intervention for lung cancer survivors; (2) control group of lung patients using usual care and exercise; (3) clinical RCTs; and (4) outcome indicators included at least one of the following: 6-min walk (6MWT), quality of life, and anxiety. | 6 -Baduanjin;<br>2 -taiji;<br>1 -yoga;<br>1 -Wuqinxi;<br>1 -qigong | The results indicated that compared to the usual care group, lung cancer patients in the mind–body exercise group could increase the 6-min walk distance (5 studies, 346 participants, WMD: 18.83, 95% CI (7.55, 30.10) P=0.001), reduce anxiety levels (4 studies, 362 participants, SMD: −1.51, 95% CI (−1.74,−1.27), p<0.05), and enhance the overall QoL (6 studies, 594 participants, SMD: 0.71, 95% CI =0.10-1.31), p=0.02) | |

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| | OR “LungCancer*” OR “Pulmonary Cancer* | | | | |
| Rogers-Shepp, 2023 (17)<br><br>Advanced cancer palliative care<br><br>8 studies | April 2022<br><br>Pubmed/Medline, Embase, CINAHL, PsychInfo, and Web of Science<br><br>MeSH terms “palliative cancer,” “palliative carcinoma,” “advanced cancer” and “palliative care” each in combination with the MeSH terms “exercise” and “exercise therapy.” | Participants had advanced cancer/metastatic cancer (stage IV) and would be considered palliative care patients (i.e. limited life expectancy but prognosis likely to be greater than 6 months)<br><br>“Exercise interventions” as a lifestyle intervention, which in principle participants could learn to do on their own at home<br><br>RCTs, physical symptoms, mental, emotional, or spiritual symptoms, and quality-of-life. | Aerobics (n = 3),<br><br>Resistance exercise and aerobics (n = 4),<br><br>Resistance exercises (n = 1) | 8 studies included<br><br>1 aerobics study had positive effect on QoL and physical function no other studies found any improvement in QoL | Rief 2014<br>Cheville 2013<br>Oldervoll 2011<br>Cormie 2013<br>Uster 2018<br>Ligibel 2016<br>Headley 2004<br>Dhillon 2012 |
| Pruchnicki, 2023 (18)<br><br>Non-small cell lung cancer<br><br>Post treatment<br><br>14 studies | December 2019<br><br>PubMed, CINAHL, and Scopus<br><br>lung neoplasms [MESH] or lung cancer* [ti/ab] or lung neoplasm* [ti/ab] or lung carcinoma* [ti/ab] or lung tumor* [ti/ab] or lung tumour* [ti/ab], AND exercise [MESH] or exercise therapy [MESH] or exercise* [ti/ab] or physical therapy modalities [MESH] or physiotherap* [ti/ab] or physical therap* [ti/ab] or physical activit* [ti/ab] or physical train* [ti/ab] | (1) The study was an RCT, (2) subjects were undergoing treatment for NSCLC, and (3) a therapeutic exercise intervention was performed | Duration of exercise intervention ranged from 3 days to 20 weeks, with the majority of studies using 8 or 12-week programs.<br><br>Mean duration of exercise sessions was 31.88 minutes (range = 5-60 minutes)<br><br>Average of 4 times a week (range = 1-14 sessions per week).<br>All studies incorporated aerobic exercise (walking or cycling) while only 9 of the 16 included strength training | Of 16 studies in the review, 13 assessed HRQoL<br><br>8 reported no difference between groups, 5 reported improvements<br><br>14 assessed exercise capacity<br><br>8 reported a significant improvement between groups, while 6 did not | Arbane 2011<br>Arbane 2014<br>Brocki 2014<br>Cavalheri 2017<br>Dhillon 2017<br>Edbrooke 2019<br>Edvardsen 2015<br>Henke 2014<br>Hoffman 2017<br>Hwang 2012<br>Messaggi-Sartor 2019<br>Sahli 2015<br>Stigt 2013 |

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| Paul, 2023 (19)<br><br>Intra-abdominal cancers<br><br>Post treatment<br><br>5 RCTs | March 2023<br><br>OVID Medline, OVID Embase, OVID Emcare, EBSCOhost CINAHL, ProQuest BNI, PubMed, and Cochrane databases<br><br>The searches included various post operative terms and exercise terms and abdominal cancer terms and surgical terms. | Adult patients over the age of 18 years with an abdominal malignancy. Patients undergoing any mode (i.e. open, laparoscopic, robotic, etc.) of resectional surgery with curative intent. Postoperative exercise programme (inpatient, outpatient or mixed) with an aerobic exercise training component. A reported outcome of cardiorespiratory fitness. Studies that compare either pre- and postoperative measures or compare an exercise group to control. | 5 RCTs all with an aerobic and resistance<br>1 aerobic only<br><br>4-12 weeks duration<br><br>Most used questionnaire was the SF-36 followed by the EORTC-QLQ C30 | Impact on health-related quality of life was variable across studies and times | Simonsen 2020<br>Porserud 2014<br>Nusca 2021<br>Gillis 2014<br>Carli 2020<br>Chang 2019 |
| Nguyen, 2023 (20)<br><br>Advanced Stage Lung Cancer<br><br>During or post treatment<br><br>12 studies | March 2022<br><br>PubMed, MEDLINE, and Cochrane | Prospective studies published in English between January 2012 to March 2022<br>patients, diagnosed with either non-small-cell lung cancer stage III–IV and/or limited disease or extensive small-cell lung cancer;<br>any exercise intervention or deliberate physical exertion<br>Studies assessing QoL, symptoms, and/or any functional status | 5- aerobic exercise alone<br>4 -mixed exercise regimen including a combination of aerobics, strength, relaxation, and/or endurance<br>2- relaxation exercises and inspiratory muscle training<br>1- three-arm study comparing two forms of aerobic exercise combined with strength training and tai chi | A significant increase in the 6MWD test was seen in three of 6 studies.<br>2 studies found significant increases in QoL and<br><br>Results support that exercise is safe and feasible with evidence supporting improved QoL and symptom mitigation | Rutkowska 2019<br>Rutkowska 2021<br>Cheung 2021<br>Dhillon 2017<br>Egegaard 2019<br>Hwang 2012<br>Kirca 2021<br>Quist 2020<br>Zhang 2016<br>Molassotis 2015<br>Bade 2021<br>Henke 2014 |
| Nelson, 2023 (21)<br><br>Breast cancer (9 studies)<br>Mixed cancer (9 studies)<br><br>18 studies | October 2022<br><br>PubMed, EMBASE, Medline Ovid, CINAHL and Pedro<br><br>MESH search terms (cancer OR tumour OR tumor OR carcinoma OR lymphoma OR leukemia OR neoplasm) and (active treatment OR | RCTs, non-RCTs, clinical trials and qualitative studies published in English that evaluated the effectiveness of dance programmes on people living with cancer. There was no time restriction applied to ensure inclusion of all available literature.<br>*Population:* people with any type and any stage of cancer who were undergoing active | Frequency varied from 1-5 times per week,<br>Sessions lasted between 30 and 90 min.<br>Intensity was omitted by most studies.<br>Duration varied from 5 to 52 weeks, resulting in a total dosage ranging between 10 and 81 hours.<br>Three studies achieved >150 min of activity per | Dance resulted in significant improvements in functional capacity (40.66 points, 95% CI 8.95–72.36; $p = 0.01$, $I^2 = 66\%$) (3 studies)<br><br>Five studies were included in a meta-analysis and found a significant improvement in QoL in favour of dance, compared to a control group | Boing 2018<br>He 2022<br>Kaltsatou 2011<br><br>Pisu 2017<br>Szalai 2015<br>Boing 2018<br>He 2022<br>Kaltsatou 2011 |

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| 8 studies both during and post treatment<br>2 during treatment only<br>7 post treatment only<br>1 unclear | inactive treatment OR radiotherapy OR chemotherapy OR survivor) and (dance OR dance therapy OR dancing OR movement to dance, NOT dance movement therapy OR dmt). | or inactive treatment, or cancer survivors, that explored physical and psychological outcomes<br>*Intervention*: any type of dance intervention<br>*Comparison*: compared dance to another intervention or to a control group. | week, 6 studies achieved 100–150 min per week and 4 achieved <100 min per week. Three studies did not include enough information. | (1.27 points, 95% CI 0.40–2.14; p = 0.004, $I^2$ = 91%) | |

6MWD: 6-Minute Walk Distance; 6MWT: 6-min Walk Test; ADL: Activities of Daily Living; ADT: Androgen Deprivation Therapy; AE: Aerobic Exercise; APA: Adapted Physical Activity; BC: Breast Cancer; BMD: Bone Mineral Density; BP: Blood Pressure; CG: Control Group; CI: Confidence Interval; CNKI: China National Knowledge Infrastructure; CPET: Cardiopulmonary Exercise Testing; CRC: Colorectal Cancer; cm: centimeter; dL: deciliter; EORTC-QLQ C30: European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire; EORTC-QLQ-CR29: EORTC-QLQ-Colon Cancer–specific Module; EQ-VAS: EuroQol-visual analogue scale; ES: Effect Size; FACT-B: Functional Assessment of Cancer Therapy-Breast instrument; FACT-G: Functional Assessment of Cancer Therapy-General instrument; FACT-P: Functional Assessment of Cancer Therapy-Prostate instrument; FITT: Frequency, Intensity, Time and Type; g: gram; HIIT: High-intensity Interval Training; Hr: Hours; HR: Heart Rate; HRQoL: Health-related Quality of Life; HRR: Heart Rate Reserve; HSCT: High-dose Stem Cell Transplant; $I^2$ : Heterogeneity; IF: Intensive Follow-up; IQR: Interquartile Range; JME: Joint Mobility Exercise; kg: kilogram; LC – Lung Cancer; m: meter; MA: Meta Analysis; MD: Mean Difference; MeSH: Medical Subject Headings; mL: millilitre; Min: minutes; MM: Multiple Myeloma; MVPA: Moderate-to-vigorous Intensity Physical Activity; NSCLC: Non-small Cell Lung Cancer; OR: Odds Ratio; PA: Physical Activity; PCa: Prostate Cancer; PHET: Preoperative Home-based Exercise Training; PRE: Progressive Resistance Exercise; PS: Performance Status; QoL: Quality of Life; QoL-CSV: QOL-Cancer Survivor Version; RBC: Red Blood Cells; RCT: Randomized Controlled Trial; RD: Risk Difference; RM: Repetition Maximum; RPE: BORG rating of perceived exertion; RT: Radiation Therapy; SD: Standard Deviation; SE: Standard Error; SF-36: 36-Item Short Form Survey; SMD: Standardized Mean Difference; $SpO_2$ : Oxygen Saturation; SR: Systematic Review; µL: microliter; VAS: Visual Analogue Scale; $VO_{2peak}$ : Peak Oxygen Uptake; WBC: White Blood Cells; WHOQOL-BREF: World Health Organization QoL questionnaire; Wk: weeks; WMD: Weighted Mean Difference

**Summary of Relevant RCTs**

| Trial Name Citations (ref) | Population | Arms / Dose (n) | Outcomes | Follow-up | Results |
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| Machado, 2024 (22)<br><br>Lung cancer<br><br>Pretreatment | 41 patients awaiting LC resection (68.1±9.3 years; 68.3% male)<br><br>20 PHET patients, 21 CG patients | Preoperative home-based exercise training combined aerobic (3x at 30 min - 40 min) and resistance (2x, 6 exercises, 2-3 sets of 15 reps) exercise, with weekly telephone supervision | Primary outcome was QoL-EORTC-QLQC30<br><br>The secondary outcomes were hospital length of stay and physical performance | Baseline, before surgery, and 1 month after surgery<br><br>The mean time between the baseline assessment and surgery was 27.5±8.5 days in the CG and 28.2±7.9 days in the exercise group (p = 0.794). | A significant group × time interaction was observed for global QoL (p =0.004). Between group differences in global QoL were statistically and clinically significant before surgery (mean difference [MD]: 13.5 points; 95% CI, 2.4–24.6; p=0.019) and after surgery (MD: 12.4 points; 95% CI, 1.3–23.4; p=0.029), favoring exercise. Clinical deterioration of global QoL was reported by 71.4% of the control group compared with 30 % of the exercise patients (p=0.003). |
| Burse, 2024 (23)<br><br>Breast cancer<br><br>Post treatment | 173 participants included in this analysis, averaging 59 years of age; about 33% of the participants were Black women. | Nine resistance exercises (e.g., chest press) twice per week and moderate exercise (walking) 30 minutes most days of the week | Primary outcomes: QoL domains of social functioning, social wellbeing, emotional/mental wellbeing, and body images<br><br>SF-36<br>BIRS<br>ULL-27<br><br>Modifiable physical activity questionnaire | baseline to 12 months post baseline | Overall, there were no significant changes in the QoL scores between the intervention conditions at 12 months post baseline<br>Although these associations were not significant, exercise improved most of the QoL outcomes (emotional/mental wellbeing, social wellbeing, body image, body image as it relates to strength and health, and social barriers). In addition, the mean differences across multiple QoL outcomes were similar for Black and White women in the exercise group. This indicates that exercise can be used to improve multiple QoL domains among Black and White women.<br>There were no significant improvements in the strength and health scores at 12 months post baseline in White women (p=0.364) and Black women (p=0.928) |
| Soriano-Malonado, 2023 (24) | 60 female breast cancer survivors who had completed their core | Resistance training group; two sessions/week for | Full-body muscular strength score was the | 12 weeks | Standardized full-body muscular strength score increased significantly in the Resistance group compared to the control |

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| Breast Cancer<br><br>Post-treatment | treatments within the previous 10 years | 12 weeks plus instructions to undertake ≥10,000 steps/day<br><br>Control group ≥10,000 steps/day only | primary outcome. Secondary outcomes included secondary muscular strength outcomes, cardiorespiratory fitness, shoulder mobility, cancer-related fatigue, depressive symptoms, HRQoL, (using the FACT-B) and life satisfaction. | | group (0.718; 95% CI 0.361–1.074, p<0.001)<br><br>There was no effect on cardiorespiratory fitness, shoulder flexion, cancer-related fatigue, depressive symptoms, HRQoL, or life satisfaction. |
| Sheill, 2023 (25)<br><br>Metastatic Prostate cancer | 61 men with metastatic prostate cancer median time since diagnosis was 34 months (IQR 7–54) | Six-month moderate to vigorous intensity aerobic exercise programme comprising a weekly class and a home-based aerobic exercise programme<br><br>Standard care control arm | Quality of life was measured using the Functional Assessment of Cancer Therapy – Prostate (FACT-P) questionnaire | Baseline, at 3 months and at 6 months | No effect of exercise on quality of life (Cohen's $d = -0.082$)<br><br>Modelling results for overall physical activity scores showed no significant main effect for the group ($p$-value = 0.25) or for time ($p$-value = 0.24) |
| Ngo-Huang, 2023 (26)<br><br>Pancreatic Cancer<br><br>During Treatment | 151 patients during neoadjuvant therapy for pancreatic cancer | Arm A: Enhanced usual care<br>Arm B: prescribed aerobic and resistance exercise during neoadjuvant therapy.<br><br>Followed the recommended ≥150 minutes of moderate intensity aerobic exercise weekly plus ≥2 resistance exercise sessions weekly | Primary endpoint was a 6-minute walk distance (6MWD; ≥14 meters improvement was clinically meaningful). Secondary endpoints included additional physical function tests, health-related quality of life, and clinical outcomes | Weekly<br><br>Mean (± SD) duration of the intervention was 22 ± 10.3 weeks for Arm A and 24 ± 12.2 weeks for Arm B (p= 0.39) | Quality of life and clinical outcomes did not significantly differ between arms<br><br>6MWD improved in both Arm A (mean change 18.6±56.8 m, p=0.01) and Arm B (27.3±68.1 m, p=0.002). |

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| Morielli, 2023 (27)<br><br>Rectal Cancer<br><br>During and after neoadjuvant chemoradiation | Rectal cancer patients (N=36) were randomized to a supervised high-intensity interval training program during neoadjuvant chemoradiation followed by unsupervised continuous exercise after neoadjuvant chemoradiation or usual care<br><br>Standard long-course neoadjuvant chemoradiation consisting of 5–6 weeks of radiation therapy (45–54 Gy) with concurrent chemotherapy | During neoadjuvant chemoradiation: 3 supervised HIIT sessions/week which mostly involved uphill treadmill walking. Each HIIT session consisted of a 5-min warm-up period, eight 2-min high-intensity intervals (85% of $VO_{2peak}$) interspersed with 2-min low-intensity active recovery intervals (40% of $VO_{2peak}$), and a 5-min cool-down<br>After neoadjuvant chemoradiation, participants in the exercise group were asked to complete ≥150 min/week of unsupervised moderate-to vigorous-intensity continuous exercise. | Symptom management and quality of life<br><br>EORTC QLQ-C30 | Baseline: pre-neoadjuvant chemoradiation, post-neoadjuvant chemoradiation and pre-surgery | During neoadjuvant chemoradiation, exercise significantly worsened stool frequency (adjusted between-group difference, 25.8; 95% CI, 4.0 to 47.6; p=0.022), role functioning (adjusted between-group difference, -21.3; 95% CI, -41.5 to -1.1; p=0.039), emotional functioning (adjusted between-group difference, -11.7; 95% CI, -22.0 to -1.4; p=0.028), and cognitive functioning (adjusted between-group difference, -11.6; 95% CI, -19.2 to -4.0; p=0.004) compared to usual care.<br>There was no between-group difference for global health status/QoL (adjusted between-group mean difference, -4.1; 95% CI, -18.3 to 10.2; p=0.56; d=-0.21).<br><br>After neoadjuvant chemoradiation, exercise significantly worsened diarrhea (adjusted between-group mean difference, 1.2; 95% CI, 0.1 to 2.3; p=0.030; d=0.59) and embarrassment (adjusted between-group mean difference, 19.7; 95% CI, 7.4 to 32.1; p=0.003; d=0.68) compared to usual care<br>No other differences were observed for the functional domains of QoL or for global health status/ QoL (adjusted between-group mean difference, 3.3; 95% CI, -10.3 to 16.9; p=0.62; d=0.17) |
| Mazzoni, 2023 (28)<br><br>Mixed cancers<br><br>During curative cancer treatment | 577 participants diagnosed with breast (78%), prostate (19%), or colorectal (3%) cancer were randomized to 6 months of exercise during curative cancer treatment moderate-to-vigorous intensity physical activity | The program consisted of a total of 6 machine-based exercises and was performed twice a week. Participants alternated between 3 × 6 repetitions maximum (RM) and 3 × 10 RM in the high intensity groups, and 3 × 12 repetitions at 50% of 6 RM and 3 × 20 repetitions at 50% of 10 | Accelerometer-assessed physical activity and outcome data (i.e., cancer-related fatigue, HRQoL, anxiety and depression, functioning in daily life, cardiorespiratory fitness, sedentary time and sleep) | Immediately post-intervention and at 12-month follow-up | For long-term activity patterns, compared to the participants in the “Low & Decreasing” category, those in the “High & Increasing” category reported significantly lower fatigue in 3 domains (general fatigue [β = −1.77], physical fatigue [β = −3.36] and reduced activity [β = −1.58]), higher HRQoL (β = 6.84) and had less sedentary time (β = −1.23)<br><br>A daily increase of 30minutes MVPA at 12-month follow-up was significantly associated with higher cardiorespiratory |

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| | Four categories with different long-term activity patterns were created: High & Increasing, High & Decreasing, Low & Increasing, and Low & Decreasing | RM in the low to moderate groups. The endurance training was home-based and consisted of 2x-weekly interval training (20-40 minutes/session) at 80–90% of heart rate reserve (HRR) in the high intensity groups, and 150 minutes weekly continuous-based exercise at 40–50% of HRR in the low to moderate intensity groups plus behavior change support | | | fitness (β=0.34, 95% CI [0.06-0.62], P=.016) and less sedentary time (β=−35, 95% CI [−0.44 to −0.27], p<0.001) |
| Malik 2023 (29)<br><br>Mixed cancers<br><br>During and after radiation therapy | 100 patients (50 patients with short-term intervention period of 3 months) (Group A) and 50 patients control group (Group B). Cancers: head and neck (20), cancer breast (15), cancer cervix (13), and cancer prostate (2) | Exercise training of 20 min moderate intensity exercise per day | $SpO_2$, Pulse Rate, and Endurance (through 6-min walk test) | 3 months<br><br>Used the QOL-CSV 2012 | Significant improvement in pulse rate, $SpO_2$ and endurance, mental health, and social dimension was found in exercising group with no significant improvement in spiritual dimension. |
| Zopf, 2022 (30)<br><br>Colorectal cancer<br><br>Post surgery | 59 patients who had undergone curative resection for colorectal cancer (stages II–III) (33 in exercise group vs. 26 in control group | Six-month supervised aerobic exercise program | Primary endpoint was cardiorespiratory fitness, measured by $VO_2$peak<br>The secondary endpoints included fatigue, QoL, and physical activity level | Baseline, 3 months, and 6 months (after the exercise intervention/ post chemotherapy)<br><br>(EORTC-QLQ-C30) and its colon cancer–specific module (EORTC-QLQ-CR29 | Relative $VO_2$peak and Wattmax improved in the exercise group compared to the control group (mean difference 4.11 ml/kg/min; 95% CI, 1.52–6.71; p=0.002 and mean difference 16.14 W; 95% CI, 5.71–26.57; p=0.003, respectively)<br><br>With regard to the EORTC-QLQ C30, a between-group difference was observed in role function in favor of the exercise group at 3 months (mean difference 19.64; 95% CI, 3.47–35.81; p=0.018; Cohen's d effect size 0.36) |
| Ochi, 2022 (31) | 50 women with stage I-IIa breast cancer, aged | Habit-B programme home-based HIIT | The primary outcome was the | 12 weeks | Intervention group had significantly larger improvement in $VO_{2peak}$ compared with |

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| Breast cancer<br><br>Post-treatment | 20–59 years who had completed initial treatment except for hormone therapy | intervention smart phone supported exercise programme for 12 weeks<br>3x per week | 12-week change in peak oxygen uptake cardiorespiratory fitness ($VO_{2peak}$). Other outcomes included muscle strength, 6min walk test, resting heart rate, physical activity, fatigue, safety and quality of life | | those in the control group (0.9 (95% CI 0.1 to 1.7) vs −0.8 (95% CI −1.5 to −0.1), p<0.01)<br><br>Some beneficial effects in terms of fatigue (ES=0.50, p=0.09) but not for physical activities or QOL<br><br>Used EQ-5D: a measure of health status from the EuroQol group 2001 |
| Mikkelsen, 2022 (32)<br><br>Older patients with advanced mixed cancers<br><br>Post treatment | 84 older adults (≥65 years) with advanced pancreatic, biliary tract, or non-small cell lung cancer who received systemic oncological treatment | 12-week multimodal exercise-based program including supervised exercise twice weekly followed by a protein supplement, a home-based walking program, and nurse-led support and counseling | Primary endpoint was change in physical function (30-second chair stand test)<br><br>Physical capacity strength, body composition, symptom burden, QoL (EORTC-QLQ-C30), symptoms of depression and anxiety, and physical activity | 13 weeks | Significant difference in change scores of 2.4 repetitions in the chair stand test, favoring the intervention group (p < 0.0001)<br><br>Statistically significant difference in favor of the exercise group for changes in global health status of the EORTC-QLQ-C30 of 13 points (SE 5.3, p = 0.020). |
| Lin, 2023 (33)<br><br>Breast cancer<br><br>Post treatment | 200 female patients who underwent surgery for BC from March to August 2021 | Control group (G0) had joint mobility exercise (JME) group; G1 was joint mobility exercise +intensive follow-up (IF) group; G2 was JME +aerobic exercise (AE)+IF group; and G3 was JME +progressive resistance exercise (PRE)+IF group. | Compare the effect of three exercise programs on lymphedema, pain, and QoL | Baseline (T1),<br>3 months post-intervention (T2), and<br>6 months post-intervention | The QOL of all patients improved over time (F=104.472, p<0.001)<br><br>T2: JME+PRE+IF resulted in the best improvement in QOL (T2: ΔG3-G0=13.032, p=0.008; T2: ΔG3-G1=13.066, p<0.001)<br><br>T3: the QOLs of both JME+ AE+IF and JME + PRE + IF group were significantly higher than that of the JME group (d=11.800, p< 0.001)<br>QOL of JME + PRE + IF group was also higher than that of JME+IF group (d=13.066, p < 0.001) |

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| Heimen, 2022 (34)<br><br>Breast cancer<br><br>Pre-surgery and post surgery | 354 stage I-III BC patients scheduled for primary surgery | Intervention group received an individual consultation with a physiotherapist and were instructed to add 30 min of daily aerobic physical activity, 2 ±1 weeks before and 4 weeks after breast cancer surgery medium intensity. resulting in shortness of breath but with the ability to talk, two follow-up telephone calls; Added physical activity was registered in a diary. | QoL<br>FACT_B; FACT_G, RAND 36; EQ-VAS, single item asking QOL in last month 0-6 | 4 weeks and 12 months | FACT-B scores at 4 weeks and 12 months showed no differences between intervention compared to control, odds ratio (OR) of 0.975 (95% confidence interval (CI) 0.636–1.495) and 0.883 (95% CI 0.581–1.342), respectively.<br><br>No difference in EQ-VAS comparing intervention to control at 4 weeks and 12 months, respectively, OR 1.163 (95% CI 0.760–1.779) and 0.817 (95% CI 0.559–1.300).<br><br>For single item QoL questions -no difference between the intervention and control group, neither at 4 weeks (OR 0.91, 95% CI 0.25–3.32) nor at 12 months (OR 1.07, 95% CI 0.30–3.86) |
| Allen, 2022 (35)<br><br>Esophagogastric cancer<br><br>Pre-surgery | 54 patients undergoing chemotherapy and surgery for esophagogastric cancer | 15-week program comprised 1 hour twice-weekly supervised exercises, 1 hour thrice-weekly home exercises, and psychological coaching<br>Aerobic, resistance and flexibility training<br><br>25 minutes bike ride; six major muscle groups were performed for two sets of 12 repetitions at RPE 12–14 | QOL, EORTC QLQ-C30;<br><br>anaerobic threshold at cardiopulmonary exercise testing CPET | CPET was performed at baseline,<br>2 weeks after neoadjuvant therapy, and<br>1 week preoperatively<br><br>QOL questionnaires were completed at baseline, mid-neoadjuvant therapy, at restaging laparoscopy, and postoperatively at 2 weeks,<br>6 weeks and<br>6 months<br><br>Skeletal muscle cross-sectional area at L3 was analyzed on | Global health status changed over time (p = 0.001) and differed between groups (p = 0.001), with a significant interaction effect (p = 0.002).<br><br>Prehabilitation resulted in an attenuated peak $VO_2$ decline (−0.4: 95% CI: −0.8 to 0.1 vs. −2.5: 95% CI −2.8 to −2.2 mL/kg/min; $p$ = 0.022), less muscle loss [−11.6 (95% CI −14.2 to −9.0) vs. −15.6 (95% CI −18.7 to −15.4) $cm^2/m^2$; $p$ = 0.049]<br><br>More prehabilitation patients completed neoadjuvant therapy at full dose (prehabilitation group, 18 (75%) vs. control group, 13 (46%); $p$ = 0.036)<br><br>For anaerobic threshold, there was no between-group difference (p = 0.574) or interaction effect (p = 0.402). |

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**Appendix 1. Members of the Expert Panel**

| Name | Affiliation | Conflict of Interest Declaration |
|---|---|---|
| Authors | | |
| Kathleen Rossini | Physiotherapist<br>Interim Clinical Lead, Oncology/Palliative Patient Care Unit<br>Credit Valley Hospital | None |
| Caroline Zwaal | Health Research Methodologist, Program in Evidence-based Care<br>McMaster University | None |
| Expert Panel | | |
| Karen Lee | Physiotherapist<br>University Health Network<br>Princess Margaret Cancer Centre | None |
| Linda Trinh | Assistant Professor, Exercise and Cancer Survivorship<br>University of Toronto | None |
| Daniel Santa Mina | Associate Professor, Prehabilitation Program<br>University Health Network | Co-founder/majority equity holder of PrehabRx which provides pre- and rehabilitation services for people undergoing surgery, including but not exclusively, people with cancer.<br>Holds numerous grants in prehabilitation and rehabilitation for people with cancer. Grants have been provided by large public agencies with mandates to support research (inc. Canadian Cancer Society, Canadian Institutes for Health Research, etc.). Has been a PI on many studies in exercise/rehabilitation in cancer. |
| Christian Lopez | PhD Candidate<br>Registered Kinesiologist<br>University Health Network | None |
| Melissa Weidman | Physical Medicine and Rehabilitation Physician<br>University Health Network | None |
| Breanna McGilvray | Regional Lead, Person-Centred Care<br>Southlake Regional Health Centre | None |
| Paty Lopez | Registered Kinesiologist<br>University Health Network | None |
| Colleen Dunphy | Manager Regional Cancer Program<br>University Health Network | None |

## DEFINITIONS OF REVIEW OUTCOMES

1. **ARCHIVE** – ARCHIVE means that a Clinical Expert and/or Expert Panel has reviewed new evidence pertaining to the guideline topic and determined that the guideline is out of date or has become less relevant. The document will no longer be tracked or updated but may still be useful for academic or other informational purposes. The document is moved to a separate section of our website and each page is watermarked with the words "ARCHIVE."

2. **ENDORSE** – ENDORSE means that a Clinical Expert and/or Expert Panel has reviewed new evidence pertaining to the guideline topic and determined that the guideline is still useful as guidance for clinical decision making. A document may be endorsed because the Expert Panel feels the current recommendations and evidence are sufficient, or it may be endorsed after a literature search uncovers no evidence that would alter the recommendations in any important way.

3. **UPDATE** – UPDATE means the Clinical Expert and/or Expert Panel recognizes that the new evidence pertaining to the guideline topic makes changes to the existing recommendations in the guideline necessary, but these changes are more involved and significant than can be accomplished through the Document Assessment and Review process. The Expert Panel advises that an update of the document be initiated. Until that time, the document will still be available as its existing recommendations are still of some use in clinical decision making, unless the recommendations are considered harmful.