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Guideline 19-5

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

Exercise for People with Cancer

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

Report Date: June 30, 2015

An assessment conducted in December 2016 deferred the review of Evidence-based Series (EBS) 19-5. This means that the document remains current until it is assessed again next year. The PEBC has a formal and standardized process to ensure the currency of each document

(PEBC Assessment & Review Protocol)

Guideline 19-5 is comprised of five sections:

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Guideline 19-5: Section 1

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

Exercise for People with Cancer: Recommendations Summary

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

Report Date: June 30, 2015

GUIDELINE OBJECTIVES

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

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

TARGET POPULATION

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

INTENDED USERS

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

PREAMBLE

The definition of exercise used in this guideline is any physical activity resulting in an increase in energy expenditure and involving planned or structured movement of the body performed in a systematic manner in terms of frequency, intensity, and duration, and designed to maintain or enhance health-related outcomes [1].

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

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

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

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

RECOMMENDATIONS

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

Guideline 19-5: Section 2

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

Exercise for People with Cancer: Guideline

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

Report Date: June 30, 2015

GUIDELINE OBJECTIVES

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

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

PREAMBLE

The definition of exercise used in this guideline is any physical activity resulting in an increase in energy expenditure and involving planned or structured movement of the body performed in a systematic manner in terms of frequency, intensity, and duration, and designed to maintain or enhance health-related outcomes [1].

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

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

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

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

RECOMMENDATIONS, KEY EVIDENCE, AND INTERPRETATION

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

Key Evidence

Safety

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

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

Quality of Life

Fourteen systematic reviews found an improvement in QoL for patients with cancer participating in an exercise intervention during the active treatment or post-treatment periods [4,6,8-21] (Table 3).

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

Muscular and Aerobic Fitness

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

Interpretation

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

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

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

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

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

Key Evidence

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

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

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

Interpretation

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

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

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

Key Evidence

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

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

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

Interpretation

Studies detected a greater and more consistent benefit when the intervention occurred in a group versus a home setting. Several systematic reviews assessed which components were included in successful interventions and concluded that the positive changes in group settings and supervised interventions were substantial.

Almost every intervention started in a supervised setting. A supervised setting may provide motivation for an individual to perform exercise. As well, it may allow for an educational component regarding safety and exercise options for individual people. This may also allow for individuals who might prefer to do exercise outside a group setting to learn about their options and to ensure that exercise professionals have the opportunity to review and instruct people on how to safely perform or use a specific modality.

6. It is recommended, where possible, that people living with cancer perform exercise at a moderate intensity (three to six times baseline resting state) on an ongoing basis, as a part of their lifestyle so that improvements in QoL and muscular and aerobic fitness can be maintained for the long term.

Key Evidence

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

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

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

Interpretation

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

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

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

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

UPDATING

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

FUNDING

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

CONFLICT OF INTEREST

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

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Guideline 19-5: Section 3

Exercise for People with Cancer: Guideline Methods Overview

The Program in Evidence-Based Care

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

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

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

Justification for Guideline

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

Guideline Developers

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

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

Guideline Development Methods

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

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

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

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

Search for Existing Guidelines

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

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

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

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

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

Guideline Review and Approval

Internal Review

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

External Review

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

ACKNOWLEDGEMENTS

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

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

Guideline 19-5: Section 4

Exercise for People with Cancer: Evidence Review

A systematic review manuscript based on this Guideline has been submitted to a peer-reviewed journal. The full Guideline will be posted here once the publication process is completed.

Guideline 19-5: Section 5

Exercise for People with Cancer: Internal and External Review

INTERNAL REVIEW

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

Expert Panel Review and Approval

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

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

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

Report Approval Panel Review and Approval

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

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

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

EXTERNAL REVIEW

External Review by Ontario Clinicians and Other Experts

Targeted Peer Review

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

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

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

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

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

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

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

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

Professional Consultation

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

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

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

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

*One blank

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

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

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

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

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

CONCLUSION

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

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

Expert Panel Members

Members	Affiliation	Conflict of interest
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Andrew Loblaw*	Radiation Oncologist Scientist, Evaluative Clinical Sciences, Odette Cancer Research Program Sunnybrook Hospital	None
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Oren Cheifetz	Physiotherapist Hematology/Oncology Program, CanWell Program Hamilton Health Sciences	None
Paul Oh	Medical Director Toronto Rehab–Cardiac Rehab Program University Health Network	None
Sara McEwen	Scientist St. John's Rehab Research Program Sunnybrook Research Institute	None
Chris Booth	Medical Oncologist Canada Research Chair in Population Cancer Care Cancer Centre of Southeastern Ontario	Yes: Study Co-chair for NCIC CTG C021
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***Working Group Member**

Report Approval Panel Members

Members	Affiliation	Conflict of interest
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Donna Maziak	Surgeon Ottawa Hospital	None
Marko Siminovic	Surgeon Juravinski Cancer Centre	None

Appendix 2. List of Abbreviations and Measures.

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

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

Appendix 3. Literature Search Strategy.

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

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

Appendix 4. AGREE II scores for included guidelines.

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

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

Appendix 5. AMSTAR results for included systematic reviews.

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

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

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

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

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

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

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

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

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

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

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