

Exercise for people with cancer: a systematic review

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ABSTRACT

Background This systematic review was completed by the Exercise for People with Cancer Guideline Development Group, a group organized by Cancer Care Ontario's Program in Evidence-Based Care (PEBC). It provides background and guidance for clinicians with respect to exercise for people living with cancer in active and post treatment. It focuses on the benefits of specific types of exercise, pre-screening requirements for new referrals, safety concerns, and delivery models.

Methods Using the PEBC's standardized approach, MEDLINE and EMBASE were systematically searched for existing guidelines, systematic reviews, and primary literature.

Results The search identified two guidelines, eighteen systematic reviews, and twenty-nine randomized controlled trials with relevance to the topic. The present review provides conclusions about the duration, frequency, and intensity of exercise appropriate for people living with cancer.

Conclusions The evidence shows that exercise is safe and provides benefit in quality of life and in muscular and aerobic fitness for people with cancer both during and after treatment. The evidence is sufficient to support the promotion of exercise for adults with cancer, and some evidence supports the promotion of exercise in group or supervised settings and for a long period of time to improve quality of life and muscular and aerobic fitness. Exercise at moderate intensities could also be sustainable for longer periods and could encourage exercise to be continued over an individual's lifetime. It is important that a pre-screening assessment be conducted to evaluate the effects of disease, treatments, and comorbidities.

Key Words Exercise, systematic reviews

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INTRODUCTION

The inclusion of exercise into an individual's daily lifestyle is known to promote many health benefits; the same holds true for people with cancer. In addition to improving physical wellbeing, exercise can help in the management of treatment side effects, and its physiologic and psychological changes can drastically affect quality of life (QOL).

The present systematic review explores the effects of exercise for people living with cancer with respect to QOL, physical fitness, safety, adverse events or injuries, intensity levels, types of exercise, and delivery models. The exercise-specific recommendations are relevant for oncologists, exercise consultants, primary care providers, and other members of health care teams who work with

people with cancer. Guidelines, systematic reviews, and primary literature are used as the evidence for the review, which was conducted for the purposes of preparing an evidence-based guideline by Cancer Care Ontario's PEBC in 2015.

METHODS

The PEBC uses the methods of the practice guidelines development cycle¹ to produce evidence-based and evidence-informed guidance documents. The process consists of conducting a systematic review, conducting a quality appraisal and interpretation of the evidence, drafting recommendations that undergo internal review, and conducting an external review.

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Literature Search Strategy for Guidelines and Systematic Reviews

A search of MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews (January 2005 to October 2013; updated to January 2014) was conducted for published guidelines and systematic reviews. The search terms "exercise guideline" and "exercise and cancer" were used in searches of the Standards and Guidelines Evidence Directory of Cancer Guidelines, the U.S. National Guideline Clearinghouse, and the Canadian Medical Association Infobase for existing evidence-based guidelines. Additional guidelines relevant to the present study were found in a general Internet search using the Google search engine. The AGREE II instrument² was used to evaluate the quality of guidelines that had relevant objectives and research questions. The AMSTAR tool³ served a similar purpose for relevant systematic reviews. Two Cochrane reviews that covered all randomized controlled trials (RCTS) until 2011 were identified. A systematic review of the primary literature was therefore conducted to update the Cochrane reviews.

Literature Search Strategy for Primary Studies

A search for primary studies in MEDLINE (September 2011 to April, week 1, 2015) and EMBASE (September 2011 to April, week 2, 2015) used the MeSH headings "exercise.mp" and "neoplasms.mp." To be included, studies had to be RCTS published in the English language between 2011 and 2015. The Cochrane Risk of Bias tool⁴ was used to assess RCTS.

Study Selection Criteria: RCTs

Articles were considered for inclusion according to their study design and relevance to the research questions. Studies were included if they were RCTS that

- considered adult individuals with cancer in active or post treatment,
- considered the effects of an exercise regimen compared with usual care,
- evaluated the outcomes of QOL and aerobic capacity or muscular fitness,
- used an exercise regimen that included repetitive aerobic or resistance exercises,
- were not included in an identified systematic review,
- were published in the English language (because of unavailability of translation services), and
- were published in 2011 or later.

Studies were excluded if they

- compared exercise regimens,
- involved non-repetitive exercise regimens (that is, yoga),
- were observational studies, or
- evaluated outcomes other than QOL or muscular or aerobic fitness.

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 data extracted from each relevant article were the

authors, publication year, study population, number of participants, treatment phase, intervention characteristics, QOL scores, fitness measures, adherence, and adverse events. All extracted data and information were audited by an independent auditor.

RESULTS

Overall Literature Search Results

The literature included in the review were 2 of the 11 identified guidelines, 18 of the 84 identified systematic reviews, and 29 of the 405 identified RCTS.

Synthesizing the Evidence

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

Outcomes

QOL and Exercise During Active or Post Treatment

A systematic review of evidence published between 2005 and 2013 identified two guidelines, eighteen systematic reviews, and twenty-nine RCTS that examined topics concerning exercise, such as safety, QOL, aerobic and muscular fitness, delivery models, and types of exercise (Figure 1, Table 1). Much of the evidence supports an improvement in QOL and physical fitness for patients participating in the interventions.

The evidence is of moderate quality (Tables II–IV). The guidelines scored well on the AGREE II reporting instrument². The systematic reviews had some issues with heterogeneity of outcomes, populations, and interventions. Issues with the RCTs included active control groups who

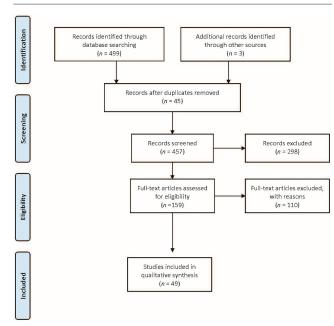


FIGURE 1 Flow diagram of study selection.

TABLE I Sources selected for inclusion

Question (exercise compared with usual care)	Sources included (n)
Does exercise improve domains of QOL?	1 Guideline ⁵ 16 Systematic reviews ^{6–21} 21 RCTs ^{22–42}
Does exercise improve physical fitness (that is, strength, VO_2 or aerobic capacity, objective measures of work done such as distance walked or sit-to-stand test)?	16 Systematic reviews ^{6–21} 16 RCTs ^{22,23,27,28,30,32,33,37,38,40,41,43–47}
What is the effect of exercise on people with cancer in terms of safety, adverse events, or injuries?	2 Guidelines ^{5,43} 3 Systematic review ^{6,7,20} 3 RCTs ^{38,39,44}
Are there differential results or outcomes for different intensity levels of aerobic compared with resistance types of exercise in people with cancer?	1 Guideline ⁴³ 7 Systematic reviews ^{6,10,11,12,18,19,48} 12 RCTs ^{22,26,29,31,33,35,39,40,42,45–47}
What delivery models are appropriate for patients with different types or stages of cancer?	4 Systematic reviews ^{8,11,15,49} 3 RCTs ^{22,36,40}

QOL = quality of life; RCT = randomized controlled trial; VO_2 = the oxygen consumed during an activity.

TABLE II AGREE II scores for the included guidelines

Domain	Score	(%)
	ACSM	KCE
Scope and purpose	72	94
Stakeholder involvement	50	58
Rigour of domain	52	81
Clarity and presentation	75	69
Applicability	31	4
Editorial independence	42	46

ACSM = American College of Sports Medicine Roundtable on Exercise Guideline for Cancer Survivors⁴³; KCE = Belgium Health Care Knowledge Centre Report 185C—Supportive Treatment for Cancer, Part 1: Exercise Treatment⁵.

increased their voluntary exercise, variation in adherence rates or lack of adherence measurements, performance bias, and in some cases, use of questionnaires targeted to patients in active treatment that might not be applicable in a post-treatment population. The next few subsections examine evidence about the safety of exercise and whether, for people with cancer, exercise can be used as an intervention to improve QOL as well as physical fitness—and, if so, what types of exercise accomplish that goal the best.

QOL and Muscular and Aerobic Fitness

For most cancer types, the Belgian Health Care Knowledge Centre⁵ found no conclusive evidence about the benefits of exercise treatment for QOL. Fourteen systematic reviews^{6–21} found an improvement in QOL for people with cancer participating in an exercise intervention during the active treatment or post-treatment periods (Table v). Of the sixteen RCTS involving patients in active treatment^{22–37}, seven reported significant differences between the intervention and control groups (Table v1)^{23,24,26,31–33,36}. In the thirteen post-treatment intervention studies^{38–53}, two reported significant QOL improvement in the exercise groups^{41,42}. In particular, patients with lymphedema experienced QOL benefits, and

aerobic and resistance exercises were both safe for women who had undergone breast and axillary surgery^{6,7,38,39,44}.

All systematic reviews^{6–21,48,49} found positive changes in both muscular and aerobic fitness (Table v). Of the sixteen RCTs that measured muscular or aerobic fitness or both^{22,23,27,28,30,32,33,37,38,40,41,43–47}, twelve found significant positive changes in the exercise groups (Table vi)^{22,23,27,28,30,32,37,38,41,43,44,46}. One systematic review¹⁴ found substantial increases in muscular strength and endurance with resistance training for patients on androgen deprivation therapy (Table v).

Safety, Adverse Events, or Injuries

The safety of exercise for adults living with cancer is a very important outcome. Safety outcomes include measures such as the frequencies and types of adverse events during exercise sessions or whether treatment delivery or cancerspecific outcomes were negatively affected.

Two guidelines^{5,43} concluded that exercise is safe for people with cancer both during active treatment and after treatment. The Belgian Health Care Knowledge Centre⁵ developed recommendations concerning the efficacy and safety of exercise treatment during cancer treatment. Based on data about the safety of exercise from a systematic literature review, no harmful effects of exercise during treatment were found. Thus, it was concluded that exercise is safe for patients undergoing treatment for cancer. The American College of Sports Medicine⁴³ convened an expert panel to create a roundtable consensus statement about exercise for cancer survivors. After reviewing the literature, the panel concluded that exercise training is safe during and after cancer treatments. They recommended that exercises could be specifically adapted based on disease- and treatment-related adverse effects such as lymphedema. They also developed pre-exercise medical assessments to help ensure safety and to guide exercise specialists concerning exercise programs for people living with cancer.

In the systematic reviews and RCTS, very few adverse events were attributable to exercise; most studies reported no adverse events at all that were attributable to exercise (Tables v and vI). Of the systematic reviews,

 TABLE III
 AMSTAR results for the included systematic reviews

	AMSTAR question								R	Reference								
		⁷ 1102 ,1a 9+ sijiuO	Ferrer et al., 2011 ¹¹	Jones et al., 2011 ⁴⁹	McMillan and Newhouse, 2011 ¹⁶	Pastakia and Kumar, 2011 ¹⁹	van Haren et al., 2011 ²¹	82102 ,.ls tə nsmusð	Fong et al., 2012 ¹³	Keogh and MacLeod, 2012 ¹⁵	Mishra et al., 2012 ¹⁸ (Active)	Mishra et al., 2012 ¹⁷ (Post)	Steins Bisschop et al., 2012 ²⁰	Cavalheri et al., 2013 ⁹	Focht et al., 2013 ¹²	Strasser et al., 2013 ⁴⁸	Cramer et al., 2014 ¹⁰	Cardner et al., 2014 ¹⁴
<u> </u>	Was an <i>a priori</i> design provided?	o N	N _o	9 N	o N	N _o	N _O	_o N	N _o	% %	Yes	Yes	%	Yes	N _o	N _o	Yes	No No
2.	Was there duplicate study selection and data extraction?	Yes and no	Yes and no	Yes	Yes and no	Yes and no	Yes	Yes and no	Yes	S _O	Yes	Yes	Yes	Yes	Yes	Yes and no	Yes	Yes
3.	Was a comprehensive literature search performed?	Yes	Yes	Yes	°Z	Yes	Yes	Yes	Yes	S Z	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4.	Was the status of publication (that is, grey literature) used as an inclusion criterion?	o Z	Yes	o Z	o Z	°Z	S Z	o Z	°Z	Yes	Yes	Yes	o Z	Yes	°Z	°Z	o Z	Yes
5.	Was a list of studies (included and excluded) provided?	°Z	Š	Š	°Z	°Z	S N	Š O	o N	Š.	Yes	Yes	Š	Yes	°Z	Yes	Yes	o N
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
۲.	Was the scientific quality of the included studies assessed and documented?	Yes and no	o Z	Yes	o Z	Yes	Yes	Yes	Yes	Yes	Yes	Yes	o Z	Yes	Yes	Yes	Yes	Yes
œ.	Was the scientific quality of the included studies used appropriately in formulating conclusions?	o Z	^o Z	Yes	o Z	Yes	Yes	Yes	Yes	Yes	Yes	Yes	o Z	Yes	Yes	Yes	Yes	Yes
.6	Were the methods used to combine the findings of studies appropriate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't answer	Yes	Yes	Yes
10.	Was the likelihood of publication bias assessed?	Yes	Yes	Yes	°Z	Yes	Yes	S S	Yes	Š	Yes	Yes	Š	Yes	S Z	Yes	Yes	o N
-	Was the conflict of interest included?	Yes	Yes	Š	Š	o Z	Š	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	S O	Yes

TABLE IV Risk-of-bias results for the included randomized controlled trials

Reference	Random sequence generation	Allocation	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcomes data	Selective reporting	Other	Comment
Arbane <i>et al.</i> , 2011 ³⁷	Low	Low	High	Low	Low	Low		Some loss to follow-up; no adherence
Anderson et al., 2012 ³⁸	Low	Low	High	Unclear	Unclear	Low	Single blinded	
Eakin <i>et al.</i> , 2012 ³⁶	Low	Unclear	High	High	High	Low		No information on pre-PA; all self-report data
Saarto <i>et al.</i> , 2012 ⁴⁰	Low	Low	High	High	Low	Low		Both groups increased exercise the same amount
Schmidt <i>et al.</i> , 2012 ⁵⁰	Unclear	Unclear	Unclear	Unclear	Low	High	Small sample size	Usual care was gymnastics; small numbers, no adherence measure
Yeo <i>et al.</i> , 2012 ³⁵	Unclear	Unclear	Unclear	Unclear	Low	Low		No information on randomization; not ITT; no info on pre-PA; no adherence measure
Andersen <i>et al.</i> , 2013 ³⁴	Low	Unclear	High	High	Low	Low		
Broderick et al., 2013 ⁴⁷	Low	Unclear	High	Low	Low		Small sample size	
Cormie <i>et al.</i> , 2013 ⁴⁵	Low	Low	High	Unclear	Low	Low	Small sample size	
Cormie <i>et al.</i> , 2013 ³⁹	Low	Low	High	Unclear	Low	Low	Small sample size	
Courneya <i>et al.,</i> 2013 ³³	Low	Low	High	High	Low	Low		
Ergun <i>et al.,</i> 2013 ⁵¹	Low	Unclear	High	Low	Low	Low	Small sample size	No information on pre-PA; no adherence measure
Hayes <i>et al.</i> , 2013 ³²	Low	Unclear	High	Low	Low	Low	Exercise group: 25% did not increase exercise	Personnel blinded for allocation or usual care group increased PA same amount as intervention group; no pre-PA
Lonbro <i>et al.</i> , 2013 ⁴²	Unclear	Unclear	High	Low	Low	Low		Control group some attrition
Mitgaard et al., 2013 ⁴⁴	Low	Unclear	High	Low	High	Low	Single blinded	High attrition
Pinto <i>et al.</i> , 2013 ⁴⁶	Unclear	Unclear	High	Low	High	Low		Personnel blinded for allocation
Rogers et al., 2013 ³¹	Low	Low	High	High	High	Low	Pilot; small sample size	
Samuel <i>et al.</i> , 2013 ³⁰	Low	High	High	High	High	High		No information on pre-PA; no adherence measure
Santa Mina et al., 2013 ²⁹	Low	Low	High	High	Low	Low	Low power	
Stigt <i>et al.</i> , 2013 ²⁸	Unclear	Unclear	High	Unclear	High	Low	Low power	Lots of dropouts; no info on pre-PA; increase in pain
Arbane <i>et al.,</i> 2014 ²⁷	Low	Low	High	High	Low	Low		
Backman et al., 2014 ²⁶	Unclear	Unclear	High	High	Low	High		All self-reported data
Bourke <i>et al.</i> , 2014 ²⁵	Low	Unclear	High	Low	Low	Low	Single blinded	
Brocki <i>et al.</i> , 2014 ⁵²	Low	Low	High	Low	Low	Low		Loss to follow-up
Galvao <i>et al.,</i> 2014 ⁴¹	Low	Unclear	High	High	Low	Low		Control group received PA recommendations
Oechsle <i>et al.,</i> 2014 ²⁴	Unclear	Unclear	High	High	Low	Low	Small sample size	
Porserud <i>et al.</i> , 2014 ⁵³	Low	Low	High	Low	Unclear	Low	Single blinded; small sample size	Lots of drop-outs
Cormie <i>et al.,</i> 2015 ²³	Unclear	Low	High	Unclear	Low	Low	Single blinded	No information on pre-PA; no follow-up
Winters-Stone et al., 2015 ²²	² Unclear	Unclear	High	Unclear	High	Low	Single blinded	Loss of follow-up; no info on pre-PA

PA = physical activity; ITT = intention to treat.

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Reference	Population	Diagnosis	Interventions	Main findings	Comments
Active treatment					
Mishra <i>et al.</i> , 2012 ¹⁸			Various exercise interventions:	Health-related quality of life:	
	12 Groups, 806 patients	Cancer	<12-Week follow-up	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 patients	Cancer	>12-Week follow-up to 6-month follow-up	SMD: 1.25; 95% CI: -0.03 to 2.53; $p=0.055$; $l^2=97\%$	
	4 Studies, 282 patients	Cancer	6-Month follow-up	SMD: 0.14; 95% CI: -0.11 to 0.39; $p=0.26$; $I^2=0.0$ %	
	21 Groups, 1166 patients	Cancer	<12-Week follow-up	SMD: 0.33; 95% CI: 0.12 to 0.55; <i>p</i> =0.0024; <i>f</i> ² =68%	Overall quality-of-life follow-up values
	8 Groups, 529 patients	Cancer	>12-Week follow-up to 6-month follow-up	SMD: 0.25; 95% CI: 0.07 to 0.43; p =0.0064; l^2 =0.0%	
	8 Groups, 686 patients	Cancer	6-Month follow-up	SMD: 0.13; 95% CI: -0.09 to 0.35; <i>p</i> =0.25; <i>l</i> ²=45%	
	3 Studies, 224 patients	Breast cancer	≤12-Week follow-up	SMD: -0.37 ; 95% CI: -1.93 to 1.20 ; $p=0.65$; $I^2=0.0\%$; $p=0.59$	
	2 Studies, 81 patients	Breast cancer	6-Month follow-up	SMD: 0.24; 95% CI: -1.60 to 2.08; p =0.79; I^2 =0.0%; p =0.35	
	4 Studies, 242 patients	Prostate cancer	≤12-Week follow-up	SMD: 0.41; 95% CI: 0.15 to 0.67; p =0.0023; I ²=0.0%; p =0.74	
	2 Studies, 121 patients	Prostate cancer	>12-Week up to 6-month follow-up	SMD: 0.28; 95 % CI: -0.10 to 0.65; p =0.15; I^2 =0.0%; p =0.96	
Carayol <i>et al.,</i> 2013 ⁶	12 Groups, 9 studies; 1390 patients	Breast cancer	Various exercise regimens were mixed: aerobic, stretching, resistance training	Quality of life: Effect size: 0.343; 95% CI: 0.067 to 0.620; p=0.015; \$I^2=73%; p<0.0001 Regression analysis investigating weekly and total exercise dose revealed significant linear models for quality of life (linear regression; number of SMD: 12; F=9.96, p=0.01; R²=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; R²=0.29	■ Lower to moderate doses of exercise (<12 MET-hours weekly) consisting of approximately 90–120 minutes of weekly moderate physical exercise seems more efficacious than higher doses in improving quality of life
Cavalheri <i>et al.,</i> 2013 ⁹	3 Studies,	After lung resection for non-small-cell lung cancer	Various exercise interventions	Quality of life: SMD: 0.17; 95% CI: -0.16 to 0.49; p =0.32; l^2 =24%; p =0.27 The mean range for health-related quality of life for the control groups was 42.2 to 73.1; for the intervention groups, it was 0.17 higher (0.16 lower to 0.49 higher). Exercise capacity: SMD: 50.35; 95% CI: 15.45 to 85.24; p =0.005; l^2 =0%; p =0.59	 3 Measures of health-related quality of life: EORTC QLQ-C30, SGRQ, SF-36 3 Different types of exercise: Small number of patients Different exercise regimens Assessed at different times

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Reference	Population	Diagnosis	Interventions	Main findings	Comments
Active treatment continued					
Van Haren <i>et al.</i> , 2013 ²¹	3 Studies, 148 patients	Hematopoietic stem-cell transplantation	Inpatient exercise regimens: some aerobic, some resistance training or structured program All used EORTC QLQ-C30	Quality of life: WMD: 8.72; 95% CI: 3.13 to 14.31; p=0.002; I²=0%; p=0.68	 Assessments at discharge
Gardner <i>et al.,</i> 2014 ¹⁴	10 Studies, 565 patients RCTs and pre–post studies	Prostate cancer with ADT	Various exercise interventions	5 RCTs and 4 UCTs included quality-of-life measures 4 Studies found significant or clinically meaningful benefits on quality of life with exercise training; 5 studies observed no effect. Resistance training consistently provided substantial increases in muscular strength and endurance; smaller improvements with aerobic training.	Appropriately prescribed exercise is safe and may ameliorate a range of treatment-induced adverse effects
Active and post treatment					
Jones <i>et al.,</i> 2011 ⁴⁹	6 Studies, 571 patients	Cancer	Various exercise interventions	${\rm VO}_{\rm 2peak}$; WMD: 2.90; 95% CI: 1.16 to 4.64; p =0.001; l^2 =87%; p <0.00001	 Looked at effects of supervised training on VO_{2peak}
	3 Studies, 86 patients	Cancer	After treatment	VO $_{\rm 2peak}$; WMD: 3.36; 95% CI: 2.20 to 4.53; p <0.00001; I^2 =0%; p =0.93	
	2 Studies, 363 patients	Cancer	During treatment	VO $_{\rm 2peak}$; WMD: 1.21; 95% CI: 0.50 to 1.92; p =0.0008; I^2 =0%; p =0.48	
McMillan et al., 2011 ¹⁶	15 Studies, 1061 patients	Cancer	Various exercise interventions	Aerobic fitness: SMD: 0.42; 95% CI: 0.32 to 0.51; p <0.001; $\chi^2_{(12)}$ =20.9; p <0.05	 Most studies had moderate-intensity aerobic or resistance exercise
	5 Studies, 419 patients	Cancer		Musculoskeletal fitness: SMD: 0.38; 95% CI: 0.18 to 0.59; $p>0.001$; $\chi^2_{(4)}=8.46$; $p>0.05$	

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Comments		Developed recommendations for an exercise program	 Developed recommendations for an exercise program regarding pelvic floor or sphincter training, and resistance or endurance exercise: aims, start, duration, session length, intensity, and so on. Only 7 studies evaluated resistance or aerobic training programs; other pelvic floor or sphincter training 	 Grade A recommendations were given if supported by at least one level 1 study Grade B recommendations were given when supported by at least one level 2 study Grade C recommendations were given when supported by any non-RCT level 3–5 studies
Main findings		Summarized the interventions used Mode: all trials included a warm up and cool down with an element of flexibility in the program: 1 used repeated limb movements with a chair 1 used a combination of aerobic and strengthening 1 used only strength 2 used a combination of aerobic and strengthening 1 used only strength 2 used a combination of aerobic and strengthening 2 used on low weights and high repetitions 2 used 60-minute session 4 progressed from 14–35 minutes 1 did not report Frequency: 7 3 times weekly 1: 3 times weekly 1: 3 times weekly during 3 cycles of chemotherapy Intensity (aerobic): 4 used 25%–85% maximum heart rate 2 used 50%–70% of 1 repetition maximum 2 used 60%–70% of 1 repetition maximum 2 used 50%–80% VO _{2max} 1 used moderate level Delivery and location: all programs were gym-based and under supervision of physiotherapist	Supervised exercise is more effective than non-supervised exercise. Recommends pelvic exercises and aerobic and resistance training to improve muscular strength, aerobic fitness, and quality of life	For overall quality of life: Crade A recommendation for group-based exercise, resistance training Crade B recommendation for aerobic training For health-related quality of life: Where the sistance plus aerobic training and resistance plus aerobic training May recommendations for group-based exercise for improvements in muscular and aerobic endurance
Interventions		Only RCTs with positive results 4 Trials used FACT-B measures Implemented between 5 weeks and 6 months	Physical activities or exercise interventions	Ranked studies into levels 1–5 (RCT>100, RCT<100, etc.), then graded recommendations based on levels and a summary of the studies. Studies used EORTC QLQ-C30 and SF-36
Diagnosis		Breast cancer	Prostate cancer	Cancer
Population	tinued	9 Studies	21 Studies, 2118 patients	12 Studies, 498 patients All study designs
Reference	Active and post treatment continued	Pastakia <i>et al.,</i> 2011 ¹⁹	Baumann <i>et al.,</i> 2012 ⁸	Keogh <i>et al.,</i> 2012 ¹⁵

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Reference	Population	Diagnosis	Interventions	Main findings	Comments
Active and post treatment continued	pən				
Steins Bisschop <i>et al.</i> , 2012 ²⁰	28 Studies, 1158 patients	Cancer	Use of cardiopulmonary exercise testing in cancer patients by continuous gas exchange analysis	Use of cardiopulmonary exercise Cardiopulmonary exercise testing was used successfully a 6 Adverse events but only 55% of testing in cancer patients by for exercise programs before, during, and after cancer studies mentioned adverse events continuous gas exchange analysis treatment. Adverse events occurred in only 1% of testing.	■ 6 Adverse events but only 55% of studies mentioned adverse events
Focht <i>et al.</i> , 2013 ¹²	15 Studies, 1077 patients	Cancer	Resistance exercise	Quality of life: Cohen d =0.25; range: -0.72 to 1.14 Muscular strength: Cohen d =0.86; range: 0.11 to 2.45 Muscular endurance: Cohen d =1.88; range: 0.66 to 2.90	
Strasser <i>et al.,</i> 2013 ⁴⁸	9 Studies, 752 patients 9 Studies, 719 patients 2 Studies, 231 patients 2 Studies, 1111 patients	Cancer Cancer Cancer	Resistance training	Upper limb muscle strength (kg): WMD: 6.90; 95% CI: 4.78 to 9.03; p<0.00001; $P=79\%$ Lower limb muscle strength (kg): WMD: 14.57; 95% CI 6.34 to 22.80; p =0.0005; P =91% VO _{2max} : VMD: 0.97; 95% CI: -0.53 to 2.47; p =0.20; P =0 12-Minute walk test: WMD: 143.65; 95% CI: 70.46 to 216.83; p =0.0001; P =0.00001; P =0.0001; P =0.0001; P =0.00001; P =0.0001; P =0.00001; P =0.0001; P =0.0001; P =0.0001; P =0.0001; P =0.0001; P =0.0001; P =0.00001; P =0.0001; P =0.001	 Resistance training only
Post treatment					
Duijts <i>et al.,</i> 2011 ⁷	12 Studies, 1699 patients	Breast cancer	Various exercise interventions	Health-related quality of life Effect size: 0.298; 95% CI: 0.12 to 0.48; p <0.001; Cochran Q (p =0.001), publication bias (p =0.034)	 Regression detected heterogeneity for health-related quality of life because of follow-up time and whether the intervention consisted of individual or group sessions
Ferrer et al., 2011 ¹¹	81 Studies 21 Studies 53 Studies 10 Studies	Cancer Cancer Cancer	Various exercise interventions	Quality of life: studies with immediate follow-up: WMD: 0.34; 95% CI: 0.25 to 0.43; 7²–69% Weighted least-squares multiple regression, >26 weeks intervention plus 4 METs All intervention groups: Cohen d=0.22; 95% CI: 0.17 to 0.28 High-quality studies: Cohen d=0.16; 95% CI: 0.010 to 0.22 >26 week intervention plus 8 METs All intervention groups: Cohen d=1.46; 95% CI: 0.90 to 2.03 High-quality studies: Cohen d=1.40; 95% CI: 0.50 to 2.29 Intervention efficacy increased when the exercise was supervised (β=-0.26, p<0.01) Quality of life: studies with delayed follow-up (3 months) WMD: 0.42; 95% CI: 0.23 to 0.61; p^2 =76% Quality of life: RCTS only, immediate follow-up: WMD: 0.24; 95% CI: 0.12 to 0.35; p^2 =66% Quality of life: RCTS only, delayed follow-up: WMD: 0.24; 95% CI: 0.058 to 0.46; p^2 =36% Quality of life: RCTS only, delayed follow-up: WMD: 0.20; 95% CI: -0.058 to 0.46; p^2 =36%	

TABLE V Continued

Comments

Main findings

Interventions

Diagnosis

Population

Reference

Post treatment continued					
Mishra <i>et al.</i> , 2012 ¹⁷			Various exercise interventions	Health-related quality of life:	
	11 Studies, 826 patients	Cancer	<12-Week follow-up	SMD: 0.48; 95% CI: 0.16 to 0.81; p =0.0032; I 2=78%	Overall quality-of-life change score
	3 Studies, 181 patients	Cancer	>12-Week follow-up to 6-month follow-up	SMD: 0.14; 95% CI: 0.38 to 0.66; p =0.61; I^2 =64%	
	2 Studies, 115 patients	Cancer	6-Month follow-up	SMD: 0.46; 95% CI: 0.09 to 0.84; <i>p</i> =0.014; <i>I</i> ²=0.0%	
	16 Studies, 760 patients	Cancer	<12-Week follow-up	SMD: 0.49; 95% CI: 0.24 to 0.74; <i>p</i> =0.00011; <i>l</i> ² =62%	 Overall quality-of-life values
	5 Studies, 353 patients	Cancer	>12-Week follow-up to 6-month follow-up	SMD: 0.11; 95% CI: -0.10 to 0.32; $p=0.32$; $I^2=0.0$ %	
	2 Studies, 115 patients		6-Month follow-up	SMD: 0.25; 95% CI: -0.12 to 0.62; $p=0.18$; $I^2=0.0$ %	
	2 Studies, 205 patients	Breast cancer	<12-Week follow-up	SMD: -0.13 ; 95% CI: -0.41 to 0.14 ; $p=0.34$; $l^2=0.0\%$; $p=0.36$	
	1 Study, 52 patients	Breast cancer	>12-Week up to 6-month follow-up	SMD: 0.99; 95% CI: 0.41 to 1.57; p=0.00084	
	2 Studies, 110 patients	Breast cancer	6-Month follow-up	SMD: 0.14; 95% CI: -0.24 to 0.51; $p=0.47$; $l^2=0.0\%$; $p=0.57$	
	1 Study, 93 patients	Colorectal cancer	>12-Week up to 6-month follow-up	SMD: -0.20; 95% CI: -2.10 to 1.70; p=0.84	
Fong <i>et al.,</i> 2012 ¹³	2 Studies, 692 patients		Various exercise interventions	Quality of life (SF-36 mental health): SMD: 2.4; 95% CI: 0.7 to 4.1; p=0.01; 1²=0%	1 Study had 641 patients; the other had 51 patients
	5 Studies, 147 patients			6-Minute walk test: SMD: 29; 95% CI: 3 to 55; p=0.03; l²=20%, p=0.288	
	7 Studies, 388 patients			VO $_{\rm 2peak}$ (mL/kg/min): SMD: 2.2; 95% CI: 1.0 to 3.4; p <0.01; l^2 =18%; p =0.29	
	3 Studies, 401 patients			Bench press (kg): SMD: 6; 95% CI: 4 to 8; p <0.01; I ² =54%; p =0.12 Leg press (kg): SMD: 19; 95% CI: 9 to 28; p <0.01; I ² =71%; p =0.03	
Cramer <i>et al.</i> , 2014 ¹⁰	3 Studies, 238 patients	Colorectal	Various exercise interventions	Quality of life: SMD: 0.18; 95% CI: -0.39 to 0.76; $p=0.53$; $l^2=59\%$, $p=0.08$ Physical fitness: SMD: 0.59; 95% CI: 0.25 to 0.93; $p<0.01$; $l^2=0\%$; $p=0.44$	Adverse events not reportedAll 3 studies used different treadmill test protocols
	i	-	-		

SMD = standardized mean difference; CI = confidence interval; MET = metabolic equivalent of task; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer quality of life questionnaire for cancer patients; SGRQ = St. George Respiratory Questionnaire; SF-36: Short Form Health Survey; WMD = weighed mean difference; RCT = randomized controlled trial; ADT = androgen deprivation therapy; UCT = uncontrolled trial; VO₂ = volume of oxygen; FACT-B = Functional Assessment of Cancer Therapy—Breast.

TABLE VI Randomized controlled trial data

Reference	Sample size	Diagnosis	Population

Active treatment

Eakin et al., 201236

68 Exercise intervention, 69 usual care

Invasive breast cancer

Women

Intervention: 16 Calls with exercise physiologist of 15–30 minutes each

- 0–2 Months: Once weekly
- 2–4 Months: Twice weekly
- 4–8 Months: Once monthly

Target of 45 minutes of moderate-to-vigorous aerobic activity, plus strength-based exercise, at least 2 times weekly (exercise workbook provided)

Frequency and Duration: 45 minutes 4 times for 8 months

Measures: Quality of life scores (FACT-B+4, score range 0–160) assessed at baseline and at 6 and 12 months post-surgery, with mean change difference at 12-months post-surgery evaluated

Main Findings:

■ Exercise group with telephone calls versus usual care: 3.7; 95% CI: –1.5 to 8.9; p=0.156

Adverse Events: No serious adverse events, but 2 minor events (muscle soreness and 1 musculoskeletal injury).

Comments:

- Telephone group had a median of 14 calls with exercise physiologist; 79% completed most calls (>75%).
- Change from baseline to 12 months post-surgery was clinically meaningful in quality of life and upper body function for exercise group only.

Andersen et al., 2013³⁴

106 Exercise intervention, 107 wait-list control Cancer

Adults receiving CTx

Intervention: 4.5 Hours high-intensity training (cardio and heavy resistance), 1.5 hours body awareness, 2 hours relaxation,

1 hour massage; usual-care group were offered an exercise program after study completion

Frequency and Duration: 9 Hours weekly for 6 weeks

Measures: Quality-of-life scores (FACT-G)

Main Findings:

Quality-of-life score

No significant difference between exercise and wait-list control group, p=0.21

Adverse Events: Not reported.

Comments:

- Self-referral of participants who were motivated to participate in group-based physical activity.
- Adherence was 75%.

Courneya et al., 2013³³

96 Aerobic exercise intervention (STAN); 101 high-dose aerobic exercise intervention (HIGH); 104 combined aerobic and resistance exercise intervention (COMB) Breast cancer

Adult women receiving CTx

Intervention

- STAN: 75 minutes vigorous aerobic exercise weekly
- HIGH: 150 minutes vigorous aerobic exercise weekly
- COMB: 75 minutes vigorous aerobic exercise weekly, plus strength-training program

Frequency and Duration:

- All participants: duration of CTx (start within 1–2 weeks and end 3–4 weeks after)
- Aerobic activity: 3 times weekly
- Strength training: 3 times weekly

 $\textit{Measures:} \quad \text{Quality of life scores (SF-36 general health), aerobic capacity (VO}_{2\text{Peak}} \text{ in millilitres per kilogram per minute),} \\ \text{and quadriceps strength (leg press in kilograms) by linear mixed-model analysis}$

Main Findings:

Mean quality-of-life score

COMB vs. STAN: -0.7; 95% CI: -2.6 to 1.1; *p*=0.44 HIGH vs. STAN: 0.6; 95% CI: -1.2 to 2.5; *p*=0.50 HIGH vs. COMB: 1.4; 95% CI: -0.5 to 3.2; *p*=0.14

Mean aerobic capacity

COMB vs. STAN: -0.2; 95% Cl: -1.2 to 0.8; *p*=0.70 HIGH vs. STAN: 0.9; 95% Cl: -0.1 to 1.9; *p*=0.08 HIGH vs. COMB: 1.1; 95% Cl: 0.1 to 2.1; *p*=0.03

Mean quadriceps strength

COMB vs. STAN: 6.0; 95% CI: 1.4 to 10.7; *p*=0.01 HIGH vs. STAN: 0.0; 95% CI: -4.6 to 4.6; *p*=0.99 HIGH vs. COMB: -6.0; 95% CI: -10.7 to -1.4; *p*=0.01

Adverse Events: No serious adverse events were related to exercise.

Comments

Higher doses of exercise were achievable and safe.

Reference	Sample size	Diagnosis	Population
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Active treatment continued

Hayes et al., 2013³²

67 Exercise group with face-to-face support, 67 exercise group with telephone support, 60 usual care Breast cancer

Adult women 6 weeks post-surgery

Intervention: Individually tailored program of 16 sessions (in person or by telephone) with exercise physiologist weekly, then tapered to monthly

- Weeks 1–4: Aerobic, low-to-moderate intensity, 20–30 minutes
- Weeks 5–8: Aerobic with strength introduced, moderate intensity, 30–40 minutes
- Week 9–32: Aerobic and strength, moderate-to-high intensity, 45 minutes or more

Frequency and Duration: By end of program, 45 minutes or more 4 times weekly using both aerobic exercise and strength-based exercise at least 2 times weekly for 8 months

Measures: Quality of life scores (FACT-B+4), aerobic fitness (change in heart rate with modified 3-minute step test), and upper-body function strength and endurance (in kilograms) at baseline and 12 months [measures were taken at pre-intervention (5 weeks), mid-intervention (6 months), and post-intervention (12 months post-surgery)]

Quality of life score

Exercise (face-to-face): 9.5; 95% CI: 5.3 to 3.8

Exercise (telephone): 13.5; 95% CI: 10.0 to 17.0 (*p*≤0.05)

Usual care: 6.5; 95% CI: 1.8 to 11.1

Face to face and telephone group experienced clinically meaningful change over time.

Significant differences between telephone group and usual care group ($p \le 0.05$)

Aerobic fitness

Exercise (face-to-face): -9.0; 95% CI: -12.9 to -5.2; $p \le 0.05$

Exercise (telephone): -6.3; 95% CI: -10.2 to -2.4; $p \le 0.05$

Usual care group: 2.7; 95% CI: –3.0 to 8.4

Face-to-face group experienced clinically meaningful change over time.

Significant differences were found between the face-to-face and telephone groups compared with the usual-care group, $p \le 0.05$

Strength and endurance

Exercise (face-to-face): 7.3; 95% Cl: 6.7 to 7.9; 9.2; 95% Cl: 8.6 to 9.8

Exercise (telephone): 6.8; 95% CI: 6.1 to 7.5; 8.3; 95% CI: 7.8 to 8.8

Usual care: 6.3; 95% CI: 5.4 to 7.2; 8.0; 95% CI: 7.1 to 9.0

All values statistically significantly different for time and group effect, p<0.05

Adverse Events: No adverse effects, events, or lymphedema were found.

Comments:

- Scheduled sessions with exercise physiologist were completed by 88% of face-to-face group and 81% of telephone group.
- Intervention goal of increasing total physical activity was not met by 25% of face-to-face and telephone groups between measures.
- In the usual-care group, 66% participated in 180 minutes or more of activity weekly, or increased their activity by 30 minutes weekly, or both.

Rogers et al., 201331

7 Exercise intervention, 8 control group

Head-and-neck cancer

Adults receiving radiation

Intervention: Resistance exercise in 2 weekly supervised sessions for 6 weeks, and 2 weekly home-based sessions; 9 different exercises using resistance bands and increasing in repetitions and band thickness as strength increased

Frequency and Duration: 1 hour 2 times weekly for 12 weeks

Measures: Quality of life scores (FACT-G) at baseline and at 6 and 12 weeks

Main Findings:

Quality-of-life score

Exercise: 73.8±14.8; 66.8±18.4; 70.6±18.2 Control: 90.4±10.8; 76.0±16.0; 84.6±13.8

Difference between groups

Baseline to 6 weeks: 7.4±14.2, *d*=0.52 Baseline to 12 weeks: 6.6±16.9, *d*=0.39

Adverse Events: No serious adverse events occurred related to resistance exercise, but 3 unrelated events occurred.

Comments:

Very small sample size

Reference	Sample size	Diagnosis	Population

Active treatment continued

Samuel et al., 201330

24 Exercise intervention, 24 usual care

Head-and-neck cancer

Adults receiving CTx

Intervention: Brisk walking 15–20 minutes at 3–5 rate of perceived exertion, and active weight program for major muscle groups of upper and lower limbs at 3–5/10 rate of perceived exertion; 8–10 repetitions for 2–3 sets

Frequency and Duration: 5 Times weekly for 6 weeks

Measures: Quality of life scores (SF-36 mental component summary) and aerobic capacity (6-minute walk distance in metres) Main Findings:

Quality of life score

Exercise: 11.73% increase Usual care: 75.21% decrease

Significant difference between groups, *p*<0.001

Aerobic capacity

Exercise: 42 m increase Usual care: 96 m decrease

Significant difference between groups, p<0.001

Adverse Events: None were found.

Comments:

Adherence not measured.

Santa Mina et al., 2013²⁹

32 Aerobic exercise intervention, 34 resistance exercise intervention

Prostate cancer

Adults receiving ADT

Intervention: Moderate- to vigorous-intensity home-based sessions, plus 1.5-hour group-based booster sessions every other week (12 sessions)

- Aerobic group: Any modality of aerobic exercise available at 60%-80% maximum heart rate, with progression (focused on walking)
- Resistance training group: 2–3 Sets of 8–12 repetitions at an intensity of 60%–80%, 1 repetition maximum, with resistance bands, exercise mat, and stability ball

Frequency and Duration: 30-60 minutes, 3-5 days weekly for 6 months

 $\label{eq:Measures: Quality of life scores (FACT-P and PORPUS), aerobic capacity (VO$_{2Peak}$ in millilitres per kilogram per minute) and grip strength (in kilograms) at baseline and at 6 months (reported as mean with standard error)$

Main Findings:

Quality-of-life score (FACT-P)

Aerobic: 123.9±3.2; 124.2±3.2

Resistance: 119.3±3.6; 117.4±4.1

Difference between groups: p=0.935

Quality-of-life score (PORPUS)

Aerobic: 67.3±2.0; 65.8±2.1

Resistance: 62.2±2.0; 62.3±2.2

Difference between groups: p=0.625

Aerobic capacity

Aerobic: 25.1±1.8; 27.9±2.0

Resistance: 28.4±1.6; 30.5±1.6

Difference between groups: *p*=0.565

Grip strength

Aerobic: 63.9±2.6; 64.5±2.7

Resistance: 69.6±2.0; 68.9±2.3

Difference between group: p=0.865

Adverse Events: There were no serious adverse events related to exercise interventions beyond the expected muscle soreness associated with novel exercise.

- Aerobic group attended 16.4% of booster sessions; 27 participants did not attend any such session.
 - Resistance group attended 5.5% of sessions; 22 did not attend any.
- Log books not completed effectively.
- No control group
- Small sample size

Reference Sample size	Diagnosis	Population
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Active treatment continued

Stigt et al., 201328

23 Exercise intervention, 26 usual care

NSCLC

Adults 4 weeks after thoracotomy

Intervention: Cycling between 60% and 80% of peak cycling load plus muscle training

Frequency and Duration: 1 hour 2 times weekly for 3 months

Measures: Quality of life scores (SF-36, general health) and aerobic capacity (6-minute walk test, metres)

Main Findings:

Quality-of-life score

No significant difference between exercise and usual care groups

Aerobic capacity

Exercise: 35 m increase Usual care: 59 m decrease

Significant difference between groups, p=0.024

Adverse Events: Not reported

Comments:

High dropout rate

Conclusion: waiting 3–4 months may be better

Increase in exercise tolerance caused more pain and physical limitations

In exercise group, only 33% of patients on ACT completed the program; 83% of patients not on ACT completed it

Backman et al., 201426

35 Exercise intervention, 36 usual care

Breast or colorectal cancer

Adults

Intervention: To walk 10,000 steps daily, plus 1 group walk for 1 hour each week; usual-care group was provided with information on physical activity

Frequency and Duration: 1 Time daily for 10 weeks

Measures: Quality of life score (EORTC QLQ-C30) at baseline and at 10 weeks

Main Findings:

Quality-of-life score

Exercise: 64.4±17.7; 59.1±18.2 Usual care: 62.9±19.1; 56.7±24.3

No significant difference between groups at the observed time points (p=0.881)

Adverse Events: Not reported

Comments:

Average of 91% adherence during intervention period

■ Exercise intervention completed by 74% of participants

Of the participants, 34% reached the goal of 10,000 steps every week

The EORTC QLQ-BR23 (breast cancer specific) found a significant difference of p=0.045 between groups.

Bourke *et al.*, 2014²⁵

50 Exercise intervention, 50 usual care

Advanced prostate cancer

Adults on long-term ADT

Intervention: Supervised aerobic and resistance exercise (aerobic: 30 minutes at 55%–75% of age-predicted maximum heart rate; resistance: training of major muscle groups), plus, in weeks 1–6, do 1 self-directed exercise session, and in weeks 7–12, do 2 self-directed exercise sessions

Frequency and Duration: 2 Times weekly for weeks 1–6, 1 time weekly for weeks 7–12 Measures: Mean difference in quality-of-life score (FACT-P) at 12-weeks and 6-months

Main Findings:

- 12 Weeks: 8.9 points; 95% CI: 3.7 to 14.2 (adjusted *p*=0.001)
- 6 Months: 3.3 points; 95% CI: 2.6 to 9.3 (adjusted *p*=0.27)

Adverse Events: One man in the intervention arm developed atrial fibrillation, and 1 death occurred in the usual care arm. No skeletal-related adverse events occurred during follow-up.

- Adherence was 94% for the supervised exercise sessions.
- Participants performed 82% of the prescribed independent exercise sessions over the first 12 weeks.

Reference	Sample size	Diagnosis	Population
Active treatment continued			
2.4			

Oechsle *et al.*, 2014²⁴ 24 Exercise intervention, 24 usual care

Acute myeloid leukemia Adults undergoing myeloablative CTx and high-dose CTx

Intervention: Individually supervised, with ergometer training (10–20 minutes) and strength exercises for major muscle groups (20 minutes) 5 times weekly while in hospital. Control group received no specific physical training, but were allowed to undergo physiotherapy as medically indicated.

Frequency and Duration: 5 Times weekly for duration of hospitalization (median duration: 21 days; range: 16–33 days)

Measures: Quality-of-life score (EORTC QLQ-C30, overall score for physical functioning)

Main Findings:

Quality-of-life score Exercise: 50Usual care: 50

Between-group difference: *p*=0.66

Adverse Events: No adverse events were found.

Comments:

- No comparison for muscle strength
- Small sample size
- No significant difference for physical function in quality of life

Cormie et al., 2015²³

32 Exercise intervention, 31 usual care

Prostate cancer

Adults receiving ADT

Intervention: Supervised group sessions involving moderate- to high-intensity aerobic (70%–85% maximum heart rate) and resistance exercises involving major muscle groups. Sessions were progressive, and participants were encouraged to supplement with home-based moderate-intensity aerobic exercise for at least 150 minutes. The usual-care group was offered the program after the study was completed.

Frequency and Duration: 1 Hour twice weekly for 3 months plus home-based 150 minutes weekly

 $\textit{Measures:} \quad \text{Quality-of-life score (SF-36 mental component summary) and aerobic capacity (VO}_{2\text{Peak}} \text{ in millilitres per kilogram per minute)} \\ \text{and quadriceps strength (leg press, 1 repetition maximum, kilograms) scores at baseline and at 3 months}$

Main Findings:

Quality-of-life score Exercise: 54.1±7.9; 56.0±6.3

Usual care: 53.1±10.0; 51.8±9.6

Difference between groups: *p*=0.022

Aerobic capacity score

Exercise: 22.1±3.5; 22.7±3.8 Usual care: 23.2±3.4; 22.7±3.6 Difference between groups: *p*=0.004

Leg press score

Exercise: 134.3±50.0; 157.9±52.9 Usual care: 143.6±52.4; 141.7±9.6 Difference between groups: p<0.001

Adverse Events: No adverse events occurred.

Winters-Stone *et al.*, 2015²² 29 Exercise intervention, 22 control group

Prostate cancer

Adults receiving ADT

Intervention: Two supervised resistance training sessions with free weights, and one home-based resistance band session weekly; control group did stretching exercises

Frequency and Duration: 3 Times weekly for 12 months

Measures: Quality-of-life score (EORTC QLQ-C30, physical functioning) and quadriceps strength (leg press, 1 repetition maximum, kilograms) at baseline and at 6 and 12 months

Main Findings:

Quality-of-life score

Exercise: 87.5±14.3; 92.2±11.7; 93.3±9.0 Control: 89.7±15.3; 82.4±20.1; 86.7±20.7 Difference between groups at 6 months: *p*<0.01

Difference between groups at 12 months: p<0.01

■ Leg press score

Exercise: 121.3 ± 33.5 ; 137.5 ± 44.3 ; 142.4 ± 52.2 Control: 119.9 ± 30.3 ; 121.8 ± 33.4 ; 120.8 ± 30.6 Difference between groups at 6 months: p=0.03 Difference between groups at 12 months: p=0.01

Adverse Events: No study-related injuries occurred.

- Retention in the study was 84% (90% in the exercise group and 75% in the control group).
- Median attendance to supervised classes was 84% in the resistance group.

Reference	Sample size	Diagnosis	Population

Post treatment

Anderson et al., 2012³⁸

52 Exercise intervention, 52 usual care

Stages I-III breast cancer

Adult women

Intervention: RESTORE (centre-based tailored moderate exercise program, with assessments at baseline and at 6, 9, 12, 15, and 18 months):

- and at 6, 9, 12, 15, and 18 months):
 0–3 Months: 2 Times weekly for 60 minutes; 20 minutes resistance training, and 30 minutes walking
- 4–6 Months: Option for home-based, 1 time weekly at centre
- 7–12 Months: Exercise at home or facility

Frequency and Duration: 65 Minutes 2 times weekly for 12 months

Measures: Mean quality-of-life scores (FACT-B) at baseline and at 18 months, and mean aerobic capacity (6-minute walk test in metres) at 18 months

Main Findings:

Quality-of-life score (mean and standard deviation)

Exercise: 102.6±16.9; 115.8±1.6 Usual care: 103.7±22.1; 114.4±2.5

No significant differences between groups: p=0.57

Aerobic capacity (mean and standard error)

Exercise: 593.2±13.0 Usual care: 558.9±11.8

The exercise group walked significantly further: *p*=0.0098

Adverse Events: 39 Adverse events occurred (7 serious), but only 2 events were deemed study-related (pectoral muscle pain and stress fracture in foot).

Comments:

- Primarily examined exercise-induced lymphedema
- Of the participants, 71.2% completed all prescribed sessions (0%–97%).
- Of the participants, 61% attended more than 75% of the sessions; 13% attended fewer than 50% of the sessions.

Saarto et al., 201240

263 Exercise intervention, 237 usual care

Breast cancer

Pre- or postmenopausal survivors

 $\label{lower} \emph{Intervention:} \quad 12 \ \text{Months of step aerobics and circuit training (BREX) in supervised 60-minute sessions (1 time weekly), and at home (2 times weekly), with a rate of perceived exertion of 14–16 (or approximately 86%–92% maximum heart rate or 76%–85% of VO_{2Max}) and 5–7 \ \text{METs}$

Frequency and Duration: 60 Minutes 3-4 times weekly for 12 months

Measures: Quality-of-life scores (EORTC QLQ-C30) and aerobic capacity (2-minute walk test in metres), evaluating the difference from baseline to 12 months

Main Findings:

Quality-of-life score

Exercise: 4.2; 95% CI: 1.9 to 6.6 Usual care: 5.6; 95% CI: 3.1 to 8.1

No significant difference between groups: *p*=0.43

Aerobic capacity

Exercise: -0.89; 95% CI: -1.03 to -0.76 Usual care: -0.72; 95% CI: -0.85 to -0.58

No significant difference between groups: p=0.15

For all participants, a significant linear trend between higher physical activity (increase in METs per week) and improved quality of life was observed (p=0.011)

Adverse Events: Adverse events were not reported.

- Adherence for supervised weekly training sessions was 62%.
- Of the participants, 88% trained for a mean of 3.2 hours weekly.
- Median number of training sessions was 3.8 weekly.
- Very active usual-care group; therefore, no difference between groups was observed.
- The exercise group increased physical activity by 3.10 MET-hours weekly. The usual-care group increased physical activity by 3.57 MET-hours weekly (approximately 17%). Increases in both groups were similar (p=0.97). All participants were also very active before the study.
- Questionnaire was not sensitive enough (for patients, not survivors).

Reference	Sample size	Diagnosis	Population

Post treatment continued

Schmidt et al., 2012⁵⁰

15 Exercise intervention, 18 usual care

Breast cancer

Adult patients

Intervention:

- Exercise group: Strength endurance training based on training load of hypothetical maximum force test (1 repetition maximum) set at 50%; a training plan was developed for each participant, with 20 repetitions during 1 training set or device (11 devices)
- Usual-care group: Weekly conventional gymnastics exercises, such as chair or floor exercises

Frequency and Duration: 1 hour 1 time weekly for 6 months

Measures: Quality-of-life scores (EORTC QLQ-C30) at baseline and at 3 and 6 months

Main Findings:

Quality-of-life score

Exercise: 59±16.6; 67±19.9; 76±12.9; *p*<0.01 Usual care: 67±17.2; 75±18.0; 77±15.3; *p*<0.01 No significant difference between groups

Adverse Events: Adverse events were not reported.

Comments:

Usual-care group in this study used conventional exercise gymnastics.

Yeo et al., 201235

54 Exercise intervention, 48 usual care

Pancreatic and periampullary cancer

Adult patients

Intervention: Every Step Counts (home walking program), with monthly diary and monthly telephone call, involving warm-up, brisk walking, and cool down (low-to-moderate intensity):

- Month 1: 5 Minutes, 10 minutes, 5 minutes
- Month 2: 5 Minutes, 20 minutes, 5 minutes
- Month 3: 5 Minutes, 25–30, minutes 5 minutes

Frequency and Duration: 3–5 Times weekly for 3 months

Measures: Quality-of-life scores (SF-36 mental component summary) at baseline and at 3 months

Main Findings:

Exercise: 45; 51 Usual care: 44; 48

Significant difference between groups: *p*≤0.05

Adverse Events: Adverse events were not reported.

Comments:

- Of the participants, 79 completed the study at final follow-up (19 months).
- Adherence not measured.

Broderick et al., 2013⁴⁷

23 Exercise intervention, 20 usual care

Cancer

Adults who completed therapy 2–6 months earlier

Intervention: Aerobic-based group sessions, plus home exercise program, working up to 75% of heart rate reserve; incremental increases in time for brisk walking at home 3–5 times weekly (usual-care group was offered an exercise program after study completion)

Frequency and Duration: 2 Times weekly plus brisk walking for 8 weeks

Measures: Quality-of-life scores (FACT-G total score) and aerobic capacity (VO_{2Peak} in millilitres per kilogram per minute) at baseline and at 2 and 3 months

Main Findings:

Quality-of-life score

Exercise: 86.2±14.8; 90.0± 12.5; 92.1±14.0 Usual care: 91.6±7.5; 95.4±11.3; 93.3±19.0

No significant difference between groups at time points: p=0.94, p=0.37

Aerobic capacity

Exercise: 19.7; 24.1; 22.8 Usual care: 19.1; 20.2; 20.4

No significant difference between groups at time points: p=0.14, p=0.61

Adverse Events: None found

- Of the participants, 60.9% attended more than 70% of group exercise classes and 78.3% met home exercise program guidelines
- Participants had very low fitness levels at start

Adult women

with cancer-related

lymphedema

TABLE VI Continued

Reference	Sample size	Diagnosis	Population
Post treatment continued			

Cormie *et al.,* 2013³⁹

22 High-load resistance exercise
intervention, 21 low-load resistance
exercise intervention, 19 usual care

Breast cancer

Intervention: 6–10 Repetitions maximum (75%–85% of 1 repetition maximum) for the high-load group or 15–20 repetitions maximum (55%–65% of 1 repetition maximum) for the low-load group (usual-care group was offered an exercise program after study completion)

Frequency and Duration: 1 hour, 2 times weekly for 3 months

Measures: Quality-of-life scores (SF-36 mental component summary), evaluating change in scores (mean with standard error)

Main Findings:

Quality-of-life score

High-load exercise: 2.9±1.7 Low-load exercise: 6.6±1.6 Usual care: 1.7±1.7

No significant difference between groups, *p*=0.195

 Significant difference between exercise groups and usual-care group for muscle endurance for chest press and seated row, but not for leg press and grip strength in affected arm.

Adverse Events: No lymphedema exacerbations or other adverse events occurred.

Comments:

- Change to the extent of swelling during the 3-month intervention did not differ between groups.
- Significant difference between groups for SF-36 physical functioning.

Cormie et al., 2013⁴⁵ 10 Exercise intervention, 10 usual care Prostate cancer Adults with bone metastases

Intervention: Resistance-based exercises of major muscle groups with an exercise specialist in groups of 1–5 (usual-care group was offered an exercise program after study completion)

Frequency and Duration: 1 Hour 2 times weekly for 12 weeks

Measures: Quality-of-life scores (SF-36 mental component summary) at baseline and 3 months

Main Findings:

Quality-of-life score

Exercise: 44.1±10.1; 42.6±12.9 Usual care: 43.5±7.2; 43.9±11.4

No significant difference between groups: *p*=0.475

Adverse Events: No adverse events or skeletal complications occurred during the supervised exercise sessions.

Comments:

■ High attendance (83%) and compliance rates (93%)

Ergun *et al.*, 2013⁵¹ 20 Supervised exercise, 20 home exercise,

20 education only

Breast cancer

Adult female patients

Intervention: Supervised exercise: aerobic exercise plus resistive exercise (upper and lower limb exercises with flexible band, moderate intensity, and brisk walking under the supervision of a specialist doctor); home exercise: brisk walking at home, moderate intensity, plus weekly telephone calls

Frequency and Duration:

- Group 1: 45 Minutes 3 times weekly for 12 weeks, plus brisk walking for 30 minutes daily, 3 times weekly for 12 weeks
- Group 2: 30 Minutes 3 times weekly for 12 weeks
- All groups: 30-Minute education program

Measures: Quality-of-life scores (EORTC QLQ-C30) at baseline and 12 weeks

Main Findings:

Supervised exercise: 67.91±16.5; 74.16±18.7; p=0.038
 Home exercise: 61.24±23.3; 68.97±21.2; p=0.489
 Control (education only): 74.58±23.5; 67.9±16.7; p=0.265
 No significant difference between groups: p=0.085

Adverse Events: No adverse effects, events or safety failures were found.

Comments.

Primary objective was to look at angiogenesis and apoptosis-related molecules.

Reference Sample size	Diagnosis	Population
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Post treatment continued

Lønbro et al., 201342

20 Early exercise intervention, 21 delayed exercise intervention Head-and-neck cancer

Adults after radiotherapy

Intervention: Progressive resistance training and self-chosen physical activity supervised 2–3 times, then left on own; telephone calls every 2 weeks to deal with training-related issues

Frequency and Duration: 30 Sessions in 12 weeks

Measures: Quality-of-life scores (EORTC QLQ-C30), evaluating change from baseline to 12 weeks

Main Findings:

Quality-of-life score

Early exercise group: 19±14 Delayed exercise group: 6±12 Between-group difference: p<0.05

Adverse Events: None found.

Comments:

Delayed group: 10 of 15 patients returned their training logs. Based on those patients, the mean training adherence rate was 98%.

Early group: 17 of 19 patients returned their training logs. Based on those patients, the mean training adherence rate was 91%.

Midtgaard et al., 201344

108 Exercise intervention. 106 health evaluation program Cancer

Adult patients

Intervention: Supervised progressive training: high-intensity aerobic interval training and resistance training of major muscle groups, plus counselling sessions (PACT)

Goal was to have participants exercise at least 3 hours weekly.

The heath evaluation group had 3 health evaluation sessions that included feedback after fitness testing and education about the health benefits of regular exercise.

Frequency and Duration: 90 Minutes 1 time weekly for 12 months

Measures: Quality of life scores (EORTC QLQ-C30), aerobic capacity (VO_{2Peak} in millilitres per minute), and quadriceps strength (leg press in kilograms) mean at baseline and at 12 months

Main Findings:

Exercise: 67.21; 95% CI: 62.70 to 71.56; 84.53; 95% CI: 80.27 to 88.36 Control: 67.16; 95% CI: 62.65 to 71.52; 81.17; 95% CI: 76.78 to 85.19 Treatment effect ratio: 1.04; 95% CI: 0.95 to 1.14; p=0.276

Aerobic capacity

Exercise: 1.97; 95% CI: 1.89 to 2.05; 2.34; 95% CI: 2.24 to 2.44 Control: 1.99; 95% CI: 1.91 to 2.08; 2.28; 95% CI: 2.18 to 2.38 Treatment effect ratio: 1.04; 95% CI: 1.00 to 1.07; p=0.032

Quadriceps strength

Exercise: 81.76; 95% CI: 76.34 to 87.57; 109.68; 95% CI: 101.98 to 117.97 Control: 84.54; 95% CI: 78.89 to 90.60; 92.84; 95% CI: 86.38 to 99.77

Treatment effect ratio: 1.22; 95% CI: 1.15 to 1.30; p<0.001

Adverse Events: Six participants in the PACT group developed lymphedema, but continued to follow the progressive resistance training without exacerbation of symptoms.

Comments:

Adherence to the weekly-supervised exercise training sessions was 66.6%.

- Heart rate during supervised exercise sessions was 77%±7% of the measured heart rate maximum.
- Significant improvements in physical activity occurred in the control group.
- High attrition rate: 24% in control group; 32% in exercise group

Reference Sample size Diagnosis **Population**

Post treatment continued

Pinto et al., 201346

20 Exercise intervention, 26 usual care

Stages I-III colorectal cancer

Adults

Intervention: Weekly calls, physical acivity counselling, home logs, and a pedometer, then monthly calls for 3 months; start at 10 minutes daily for 2 days weekly, reaching 30 minutes daily for 5 days weekly (brisk walking or use of home exercise equipment at 64%–76% of estimated maximum heart rate)

Frequency and Duration: Start: 2 times weekly; end: 5 times weekly for 12 weeks

Measures: Quality-of-life scores (FACT-C) and aerobic capacity (VO_{2Peak} in millilitres per kilogram per minute) at baseline and at 3, 6, and 12 months

Main Findings:

Quality-of-life score

Exercise: 105.3; 111.3; 111.7; 110.7 Usual care: 105.3; 110.8; 108.7; 110.6

No significant difference

Aerobic capacity

Exercise: 22.97; 27.65; 28.43; 27.06 Usual care: 22.97; 23.71; 24.36; 22.12

Significant difference between groups at time points: p=0.017 at 3 months, p=0.017 at 6 months, and p=0.002 at 12 months

Adverse Events: Adverse events were not reported.

Comments:

- 7-Day physical activity recall showed that, compared with the usual-care group, the exercise group exercised significantly more at 3 months but not at 6 and 12 months.
- No real exercise program.
- Primary outcome was increase in physical activity, with an emphasis on behavioural counselling.

Brocki et al., 201452

41 Exercise intervention, 37 control group

Lung cancer

Adult patients, surgically resected

Intervention: Supervised, group-based exercise training sessions that included aerobic exercises with a target intensity of 60%-80% of work capacity and resistance training (both groups were given home exercise instructions and training diaries)

Frequency and Duration: 1 hour 1 time weekly for 10 weeks

Measures: Quality of life scores (SF-36 version 2, mental component summary) and aerobic capacity (6-minute walk test, metres) at baseline, with change score at 4 months and 1 year

Main Findings:

Quality-of-life score

Exercise: 45.67; 4.4; 5.33

Control: 44.88; 5.4; 9.6

Between-group difference at 4 months: p=0.99 Between-group difference at 1 year: p=0.27

Aerobic capacity

Exercise: 427 m; 61 m; 65 m Control: 407 m; 55 m; 60 m

Between-group difference at 4 months: p=0.57Between-group difference at 1 year: p=0.93

Adverse Events: None found

- In the control group, 43% regularly exercised at home or joined an exercise program.
- In the exercise group, 43% reported exercising at home at least 2 times weekly.
- Supervised only once weekly.
- Lost in follow-up: 43% of exercise group and 13% of control group

Reference	Sample size	Diagnosis	Population
Post treatment continued			
Galvao <i>et al.,</i> 2014 ⁴¹	50 exercise intervention, 50 control group	Prostate cancer	Adults previously treated with ADT and radiation (>5 years)

Intervention: Combined supervised progressive group resistance training of major muscle groups and 20–30 minutes cardiovascular exercises at 70%–85% maximum heart rate, plus two aerobic exercise sessions at home each week; control group received printed materials about physical activity and a pedometer

Frequency and Duration: 4 Times weekly for 6 months, then home-based sessions for months 7-12

Measures: Quality of life scores (SF-36 version 2, mental component summary), aerobic capacity (400 m walk time in seconds), and quadriceps strength (leg extension in kilograms) at baseline and at 6 and 12 months

Main Findings:

Quality-of-life score

Exercise: 50.3 ± 9.6 ; 51.6 ± 6.6 ; 51.2 ± 7.5 Control: 47.4 ± 10.4 ; 47.1 ± 9.5 ; 48.7 ± 9.5 Between-group difference at 6 months: p=0.025 Between-group difference at 12 months: p=0.649

Aerobic capacity

Exercise: 288.0 ± 7.6 ; 269.4 ± 8.4 ; 270.4 ± 7.3 Control: 276.5 ± 7.6 ; 279.4 ± 8.4 ; 274.1 ± 7.3 Between-group difference at 6 months: p=0.029 Between-group difference at 12 months: p=0.028

Quadriceps strength

Exercise: 50.7 ± 3.0 ; 59.3 ± 3.0 ; 56.6 ± 2.8 Control: 51.0 ± 2.9 ; 49.9 ± 2.9 ; 50.2 ± 2.8 Between group difference at 6 months: p<0.001Between group difference at 12 months: p=0.011

Adverse Events: One participant with pre-existing back pain, and one with pre-existing knee injury withdrew from exercising; one died from lung cancer, and one had a nonfatal myocardial infarction.

Comments:

Physical activity recommendations given to the control group (should do more than 150 minutes of moderate activity weekly)

Porserud et al., 2014⁵³

9 Exercise intervention, 9 usual care Urinary bladder cancer

Adults after radical cystectomy

Intervention: Supervised group strength and endurance training for lower extremities, such as walking and strengthening exercises, balance, mobility, and stretching exercises; participants were also instructed to take self-paced walks for at least 15 minutes 3–5 days weekly. The usual-care group was offered the program after the study was completed.

Frequency and Duration: 45 minutes 2 times weekly for 12 weeks, plus 15 minute walks 3–5 times weekly

Measures: Quality-of-life scores (SF-36 mental health component) and aerobic capacity (6-minute walk test), evaluating increase from baseline to 12 weeks and from 12 weeks to 1 year

Main Findings:

Quality-of-life score

Exercise: 5.6±10.0; 2.4±5.6 Usual care: 2.1±16.0; 0.4±8.1

Difference between groups after training: *p*=1.00

Difference between groups at 1 year: p=0.67

Aerobic capacity

Exercise: 112.9±40.1; 23.8±8.2 Usual care: 62.8±26.3; –19.2±15.3

Difference between groups after training: *p*=0.013

Difference between groups at 1 year: p=0.010

Adverse Events: None attributable to the intervention were reported.

- Small sample size
- Many dropouts
- Exercise group attended 76%±67%–95% of group exercise sessions and took daily walks 87%±56%–100% of the days.

Reference Sample size Diagnosis Population	
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Immediately postoperative

Arbane et al., 2014²⁷

64 Exercise intervention, 67 usual care

NSCLC

Adults after curative surgery

Intervention: 1 30-minute daily cycle strength and mobility training days 1–5 post-op, and home-based walking program with weekly telephone call to encourage continued 30 minutes of walking daily (walking and strength training adapted to the patient)

Frequency and Duration: 1 Time daily for 1–5 days; when at home, 1 time daily (30 minutes of walking for 4 weeks)

Measures: Quality-of-life scores (SF-36, EORTC QLQ-LC13) and quadriceps strength (kilograms force)

Main Findings:

Quality-of-life score:

No significant differences between groups from baseline to 4 weeks after surgery.

• Quadriceps strength:

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.

Adverse Events: There were complications from surgery, but no other adverse events were reported.

Comments:

- The inpatient goals were not met because of short stay or discomfort.
- \blacksquare An airflow obstruction sub-analysis found a significant difference between groups for quality of life (p=0.01).

Arbane et al., 201137

27 Exercise intervention, 26 usual care

NSCLC

Adults referred for lung resection by open thoracotomy or visually assisted thoracotomy

Intervention: Strength and mobility training 2 times daily on days 1–5 postoperatively, and 12-week home-based program with 3 visits (once monthly) to encourage continued use of exercise program (walking and strength training adapted to patient, reaching 60%–80% of maximal heart rate)

Frequency and Duration: 5-10 Minutes to start, then adapted to individual 2 times daily for 5 days post surgery, and then for 12 weeks

Measures: 12-Week change in quality-of-life scores (EORTC QLQ-C30, global health score), and change in mean aerobic fitness (6-minute walk test in metres) and in mean quadriceps strength (magnetic stimulation of femoral nerve, kilograms) preoperatively, 5 days postoperatively, and at 12-week follow-up

Main Findings:

Quality-of-life score

Exercise: 6.5; 95% CI: -7.7 to 20.7

Usual care: 2.2; 95% CI: -5.2 to 9.6

No significant difference were observed over time or between groups.

Mean aerobic fitness

Exercise: 466.6±102.1; 336.7±84.1; 480.2±110.0

Usual care: 455.7±98.0; 308.7±124.8; 448.2±95.1

Repeated measures analysis, overall within-subject time effect: p<0.001; group effect, p=0.47

Preoperatively to 5 days postoperatively (paired t-tests): inter-subject group time effect: p=0.89

Mean quadriceps strength

Exercise: 33.2±15.2; 37.6±27.1; 34.2±9.4 Usual care: 29.1±10.9; 21.5±7.7; 26.4±9.7

Repeated measures analysis within-subject time effect: p=0.70

Preoperatively to 5 days postoperatively inter-subject group effect: p=0.04

Adverse Events: Adverse events were not reported.

Comments:

- No adherence information
- No clear intervention information after 5 days postoperatively
- Some loss to follow-up
- Many participants could not complete the quadriceps strength measures because of metal implants, and many did not repeat the quadriceps strength measures.

FACT-B[+4] = Functional Assessment of Cancer Therapy–Breast [patients with lymphedema]; CI = confidence interval; CTx = chemotherapy; FACT-G = Functional Assessment of Cancer Therapy–General; SF-36 = Short Form (36) Health Survey; VO₂ = volume of oxygen; ADT = androgen deprivation therapy; FACT-P = Functional Assessment of Cancer Therapy–Prostate; PORPUS = Patient Oriented Prostate Utility Scale; ACT = Adjuvant chemotherapy; EORTC = European Organisation for Research and Treatment of Cancer; QLQ-C30 = 30-question quality-of-life survey; QLQ-BR23 = 23-question breast cancer–specific quality-of-life survey; MET = metabolic equivalents; PACT = Physical Activity after Cancer Treatment; FACT-C = Functional Assessment of Cancer Therapy–Colorectal; QLQ-LC13 = 13-question module for lung cancer trials.

nine^{6–9,13,15,16,19,21} made no mention of adverse events, two^{10,48} indicated that no adverse events were reported in the studies, and six^{12,14,17,18,20,49} indicated that adverse events had been reported in studies, but did not provide information about the events. One systematic review²⁰ found that cardiopulmonary exercise testing was a safe, noninvasive method to measure cardiopulmonary fitness in people living with cancer, both during and after treatment.

Seventeen RCTs^{22–24,27,29,30–33,37,39,42,45,47,51–53} found that no adverse events or side effects were attributable to the exercise program. Seven^{26,28,34,35,40,46,50} did not report on adverse events at all. Three RCTs^{25,41,44} reported adverse events that were deemed not to be related to the intervention; two^{36,38} reported events that were attributable to the intervention (3 patients experienced muscle soreness, and 2 experienced musculoskeletal injury).

Delivery Models and Supervised Settings

Four systematic reviews \$\frac{8}{11},15,49\$ detected a greater and more consistent benefit of exercise for QOL and muscular and aerobic fitness when the intervention was offered in a group or supervised setting compared with a home-based or unsupervised setting (Table v). Two RCTS^{32,36} compared various settings for interventions and found that the beneficial effects were greater when exercise was supervised, either in groups or by telephone. One RCT⁴⁰ found a significant linear trend between an increase in weekly metabolic equivalents of task performed and an improved QOL score for all patients in the study.

Intensity Levels and Types of Exercise

Intensity Levels: Three systematic reviews^{6,11,18} studied exercise intensity levels and found that studies of longer length (more weeks) and those that included at least moderate-intensity exercise were associated with improved QOL and muscular and aerobic fitness (Table v). Another systematic review¹⁹ that evaluated interventions with positive results for QOL found that moderate-intensity aerobic exercise programs used in those interventions resulted in a benefit for QOL (Table v). Two RCTS^{33,39} compared various exercise intensity levels and found improvements in muscular endurance and aerobic capacity for the higher-intensity groups (Table vi). One RCT⁴⁰ found, for all participants, a significant linear trend between an increase in weekly energy expenditure or metabolic equivalents of task performed and an improved QOL score (Table vi).

Resistance Training: Focht *et al.*¹² analyzed only resistance exercise interventions used in fifteen studies in both active- and post-treatment patients, finding a small and meaningful increase in effect size for QoL (Cohen d=0.25; range: -0.72 to 1.14). In a systematic review, Cramer *et al.*¹⁰ examined resistance training in three studies with colorectal cancer patients, finding that resistance training improved colorectal cancer–specific QoL. Strasser *et al.*⁴⁸ looked at both active- and post-treatment groups in four RCTS that compared a resistance training group with a non-exercise group and that measured QoL (five other RCTS examined muscle strength): two RCTS detected a significant effect of resistance training for QoL (compared with usual

care), and two RCTS detected a trend for improved QOL in the resistance training group.

Five RCTs^{22,31,39,42,45} used resistance training alone for their exercise intervention. Winters-Stone $et\,al.^{22}$ and Lonbro $et\,al.^{42}$ both found a significant difference in QOL for the exercise group (p < 0.01 and p < 0.05 respectively). Rogers $et\,al.^{31}$ found a positive minimally important difference effect size of d = 0.52 at 6 weeks and d = 0.39 at 12 weeks. Cormie $et\,al.^{39,45}$ did not find a significant difference between groups for QOL in both of their RCTS (p = 0.195, p = 0.475).

Aerobic Training: Ferrer *et al.*¹¹ found that aerobic activity intensity was a significant predictor of QOL improvement as a quadratic trend (bivariate moderator analyses: $\beta = 0.25$, p = 0.03). Four RCTs^{26,35,46,47} used only aerobic interventions. Three^{26,46,47} showed no significant differences between the intervention and control groups for QOL, but in one³⁵, paired pre–post t-tests showed a significant difference between groups on the Short Form-36 mental component summary ($p \le 0.05$).

Resistance Versus Aerobic Training: Santa Mina *et al.*²⁹ compared aerobic and resistance training programs, both moderate-to-vigorous intensity and home-based. No difference in QOL was found between the training groups.

Pre-exercise Assessment for Evaluation of the Effects of Disease Treatments or Comorbidities: The American College of Sports Medicine's guideline expert panel developed recommendations for pre-exercise medical assessments to help ensure patient safety and to guide exercise specialists with respect to an exercise program for people living with cancer⁴³. One systematic review in the panel's literature review²⁰ found that cardiopulmonary exercise testing is a safe, noninvasive method for measuring the cardiopulmonary fitness of people living with cancer, both during and after treatment. No RCT in the literature review reported any adverse events during pre-screening or baseline assessments before initiation of the study intervention^{22–42,44–47,50–53}.

DISCUSSION

Safety, QOL, and Muscular and Aerobic Capacity

Outcomes of importance to the current guideline included safety, QOL, and aerobic and muscular fitness. Numerous studies provide evidence that supports an improvement in QOL for patients participating in the interventions. The published guidelines concluded that exercise is 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 can occur, but a cancer diagnosis or its therapy does not exert a negative influence.

Exercising in Group or Supervised Setting

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

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

Exercising at Moderate Intensity and Length of Intervention

No studies directly compared various intensities or lengths of exercise interventions for people with cancer. The systematic reviews detected a benefit for increasing intensities up to a moderate level (3–6 metabolic equivalents of task), but greater amounts of exercise did not necessarily further improve outcomes, including QOL.

Longer interventions (18 weeks and ongoing) detected a benefit for QoL as well as for aerobic and muscular fitness. Compared with high intensities, moderate intensities of exercise might be sustainable for a longer period and might encourage exercise to be continued throughout a person's life.

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

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

It is a standard recommendation that healthy adults in the general population undergo a fitness assessment before initiating exercise; people living with cancer should therefore also participate in a pre-exercise fitness assessment. The assessment should evaluate comorbidities and any possible latent effects from treatment that might alter a person's ability to safely engage in exercise. Such an assessment also allows the exercise consultant to modify an exercise program, individualizing it for the person and giving consideration to modifications of standard programs based on physical limitations or vulnerabilities.

The time and personnel required to perform a preexercise assessment are acknowledged. However, such assessments can allow clinicians and people living with cancer to feel more safe and secure before an exercise regimen commences. Assessments can also ensure that individuals are aware of potential vulnerabilities connected to their condition.

Implementation Considerations

Some of the issues identified here include concerns about the lack of exercise knowledge, funding, facilities, programs, qualified staff, and exercise specialists in cancer. Clinicians or health care professionals might be inexperienced with exercise regimens, and pre-exercise screening for all cancer survivors could be difficult to achieve, given the additional time and personnel requirements. The type of activity and exercise will depend on the individual patient and his or her preferences, and the choice should be promoted as a part of rehabilitative recovery or the survivorship phase of a treatment program.

Evidence Limitations

The present systematic review was conducted to provide a background and guidance for clinicians with respect to exercise for people living with cancer. It focuses on the benefits of specific types of exercise, pre-screening requirements for new referrals, safety concerns, and delivery models. It covers all cancer types; aerobic and resistance exercise; and QoL, muscular, and aerobic outcomes. Other reviews were more specialized in their objectives. Unfortunately, evidence to create specific exercise regimens for specific types of cancer was not available to provide guidance for clinicians. In addition, evidence that met the inclusion criteria was insufficient to produce recommendations based on survival outcomes.

The evidence found in this review showed some weaknesses. A systematic review was not undertaken to inform the guideline from the American College of Sports Medicine; that guideline depended on expert opinion for some topics (such as the pre-screening recommendation). Many of the systematic reviews had issues with heterogeneity in their analysis. Sources of heterogeneity included a population with varying cancer types; varied timing of the exercise intervention (during or after completion of therapy); varying interventions (aerobic compared with resistance training); various lengths of intervention (4–24 weeks); variable exercise intensities; varying frequencies of the intervention (daily to 2, 3, or 5 times per week); multiple measures of QoL, aerobic capacity, and strength; varying use of individual or group sessions; and variable timing of the assessments.

The risk of bias in lifestyle trials is an acknowledged issue. Within the RCTS reviewed, the following concerns were noted: participants could not be blinded; some assessments (especially QOL) were subjective; many trials had performance bias; many trials did not measure exercise activity before entry into the study; adherence during the intervention was variable or not reported; and the exercise level of the control group quite often increased during the intervention, sometimes as much as it did in the exercise group. The lengths of the RCTS were not sufficient to fully study a long-term exercise duration. The study lengths were connected to the money and time needed to complete a study rather than to the feasibility or sustainability of the exercise regimen.

CONCLUSIONS

Exercise is safe and can provide QOL and fitness benefits for adults living with cancer, whether during active treatment or after treatment. During active treatment, systematic reviews examining patients with all cancers demonstrated a positive influence of exercise on QOL. In RCTS, benefits within and between groups were found for exercise interventions of moderate intensity. For the post-treatment period, systematic reviews found a positive influence for all exercise interventions. Thus, people living with cancer can

be allowed to determine the type of exercise that they would prefer to do for aerobic and resistance training (for example, running, brisk walking, cycling, weight lifting, body weight or elastic band exercises), with similar benefits.

So far, studies have not been designed to determine more exact exercise programs for specific cancer types. Studies with a longer duration are also needed to determine the long-term effects of exercise, as are studies that compare various exercise intensities to determine any difference in benefit. In the present review, evidence that met the inclusion criteria was insufficient to provide recommendations based on survival outcomes. However, sufficient evidence is available to promote exercise to adults with cancer, and some evidence is available to promote exercise in a group or supervised setting and for a long period of time to improve QOL and muscular and aerobic fitness. Exercise at a moderate intensity might be sustainable for longer periods and could potentially encourage continuation over a lifetime. It is important that a pre-screening assessment be conducted to evaluate for the effects of disease, treatments, or comorbidities. More research to help create more exact exercise programs for specific cancer types would be beneficial.

REVIEW AND UPDATE

Practice guidelines and literature reviews developed by the PEBC are reviewed and updated regularly. For the full guideline and subsequent updates, please visit the Cancer Care Ontario Web site at https://www.cancercare.on.ca/ toolbox/qualityguidelines/clin-program/psychonc/.

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CONFLICT OF INTEREST DISCLOSURES

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

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