Are Exercise Programs Effective for Improving Health-Related Quality of Life Among Cancer Survivors? A Systematic Review and Meta-Analysis

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Purpose/Objectives: To evaluate the effectiveness of exercise interventions on overall health-related quality of life (HRQOL) and its domains among cancer survivors who have completed primary treatment.

Data Sources: 11 electronic databases were searched from inception (dates varied) to October 2011. The authors also identified eligible trials through a search of additional sources.

Data Synthesis: 40 trials with 3,694 participants met the inclusion criteria. At 12 weeks, cancer survivors exposed to exercise interventions had greater positive improvement in overall HRQOL (standardized mean difference [SMD] 0.48; 95% confidence interval [CI] [0.16, 0.81]), emotional well-being (SMD 0.33; 95% CI [0.05, 0.61]), and social functioning (SMD 0.45; 95% CI [0.02, 0.87]); and had a significant reduction in anxiety (SMD –0.26; 95% CI [–0.44, –0.07]) and fatigue (SMD –0.82; 95% CI [–1.5, –0.14]).

Conclusions: Exercise programs have a beneficial effect on HRQOL and most of its domains and can be integrated into the management plans for cancer survivors who have completed treatment. Future research is needed to help understand specific attributes of exercise programs that are beneficial for improving HRQOL within and across cancer types.

Implications for Nursing: Evidence presented in this review supports the inclusion of exercise programs in clinical guidelines for the management of cancer survivors who have completed treatment, such as the Oncology Nursing Society's Putting Evidence Into Practice resource.

Key Words: quality of life; health status; anxiety; depression; fatigue; neoplasm; neoplasm therapy; exercise; survivors; walking; yoga; resistance training; breathing exercises; bicycling; physical activity

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The growing numbers of cancer survivors and the growing length of survival following a cancer diagnosis have raised issues related to the long-term and late effects of cancer and its treatment. Long-term effects begin at the time of initial treatment and chronically persist. Examples of long-term effects include fatigue, cognitive dysfunction ("chemobrain"), and functional deficits that result from treatment (e.g., swallowing problems in patients with head and neck cancer). Examples of late effects include heart failure related to toxicity from chemotherapy and secondary tumors. Many of these long-term and late effects have an impact on patients' health-related quality of life (HRQOL). HRQOL is a multidimensional concept reflecting patients' perceptions regarding the effect of disease and treatment on their physical, psychological, and social functioning and well-being (U.S. Food and Drug Administration, 2009). Interventions to address these HRQOL issues in cancer survivors are critically needed.

One of the interventions to address cancer survivors' HRQOL that has received considerable attention is exercise. The research on the impacts of exercise on cancer survivors' quality of life has been diverse—with focus on a variety of exercise interventions (e.g., yoga, strength training, aerobics), diversity in terms of types of cancers survived, a range of times since diagnosis, and a multitude of treatments received. In addition, the specific quality of life outcomes addressed also have varied considerably, sometimes focusing on global HRQOL, general areas of functioning (e.g., physical, emotional), or specific effects (e.g., fatigue, pain). Previous systematic reviews found an improvement in HRQOL, psychological well-being, and fatigue in cancer survivors following an exercise intervention during and after cancer treatment (Cramp & Byron-Daniel, 2012; Galvao & Newton, 2005; Knols, Aaronson, Uebelhart, Fransen, & Aufdemkampe, 2005; McNeely et al., 2006; Mustian et al., 2007; Schmitz et al., 2005; Stevinson, Lawlor, & Fox, 2004; Thorsen, Courneya, Stevinson, & Fossa, 2008), but these reviews searched only one or two databases or included nonrandomized studies in addition to randomized, controlled trials (RCTs) (Galvao & Newton, 2005; Schmitz et al., 2005; Stevinson et al., 2004; Thorsen et al., 2008).

The current review, originally published as a Cochrane systematic review (Mishra et al., 2012), was conducted to answer the question: What are the effects of exercise on overall HRQOL and specific HRQOL domains among adult cancer survivors who have completed treatment?

Methods

Eligibility Criteria

The authors included trials that met the following conditions: (a) were RCTs or controlled clinical trials, (b) included only adult cancer survivors, (c) compared exercise interventions that were initiated after conclusion of cancer treatment with usual care or a non-exercise comparison intervention, and (d) measured overall HRQOL or a HRQOL domain as an outcome. Trials were excluded if they focused on terminally ill patients, those receiving hospice care, or where the majority of participants were undergoing treatment.

Exercise was defined as any physical activity that caused an increase in energy expenditure and involved a planned or structured movement of the body performed in a systematic manner in terms of frequency, intensity, and duration and was designed to maintain or enhance health-related outcomes (American College of Sports Medicine, 1998, 2005). Interventions were classified as mild, moderate, or vigorous when a quantitative assessment (i.e., rate of perceived exertion or heart rate) of exercise intensity was not available.

The patient-reported outcomes included overall HRQOL and HRQOL domains, including functioning (physical, psychological, social, and role), spiritual well-being, pain, vitality, general health perceptions, and positive attributes, and disease- and treatment-related symptoms. These outcomes were grouped into four follow-up intervals (12 weeks, more than 12 weeks but less than 6 months, 6 months, and more than 6 months following the exercise intervention). The Cochrane review (Mishra et al., 2012) lists the instruments used to measure HRQOL and HRQOL domains.

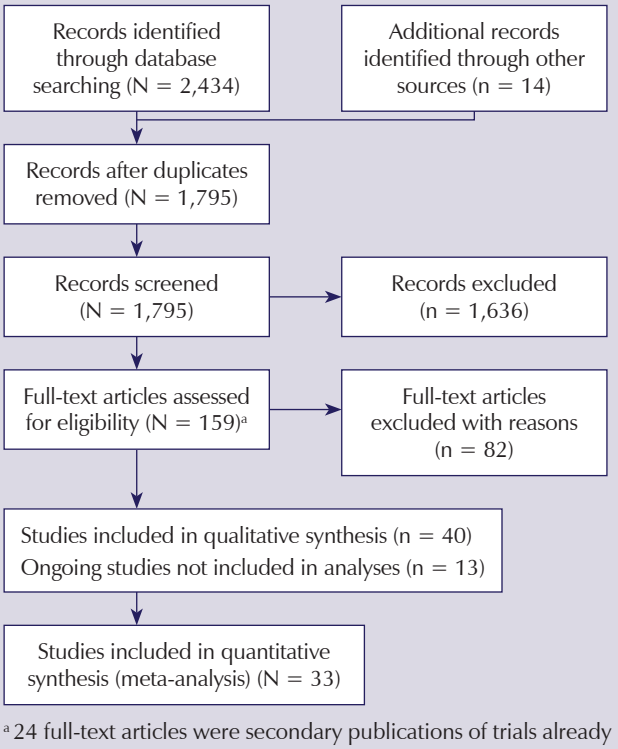
Information Sources and Data Collection

The authors searched 11 electronic databases (MEDLINE®, the Cochrane Register of Controlled Trials [CENTRAL], EMBASE, CINAHL®, PsycINFO, PEDRO, LILACS, SIGLE, SportDiscus, OTSeeker, and Sociological Abstracts) from inception (various dates) to October 2011, with no language or date restrictions. A search strategy was developed for MEDLINE and modified for the other databases. Mishra et al. (2012) contains additional details on the search strategy.

All trials were screened for eligibility based on their title and abstracts. Following that step, the authors reviewed full-text versions of trials deemed eligible or possibly eligible to confirm eligibility (see Figure 1). Paired reviewers determined eligibility of each trial and abstracted data on trial characteristics and effects of the intervention on outcomes. Disagreements between reviewers were resolved through consensus or through involvement of a third reviewer. The authors attempted to contact the original trial author to obtain missing data or seek clarity. For the included trials, based on the Cochrane handbook recommendations for judging risk of bias (Higgins, Altman, & Sterne, 2011), parameters of risk of bias were graded as high, low, or unclear. Mishra et al. (2012) contains additional details on the methodology used to select trials, abstract data, reconcile differences between reviewers, and assess risk of bias.

Data Synthesis and Analysis

Data from trials were combined in a meta-analysis when appropriate (i.e., data showing no significant clinical heterogeneity). The authors pooled all trials for a random effects meta-analysis to determine the pooled intervention effect estimate (odds ratio [OR] and 95% confidence interval [CI]). Because trial results were reported as a change in score from baseline to follow-up or follow-up values, a meta-analysis was completed for both types of measures and for each follow-up time period. In addition, the authors used a weighted mean



[a] 24 full-text articles were secondary publications of trials already included in the review.

Figure 1. PRISMA Flow Diagram of Study Selection Process

difference (WMD) when trials measured the HRQOL outcome using the same measure or scale and used a standardized mean difference (SMD) when trials measured the HRQOL outcome using different measures or scales. Differences in this type of analysis are reported in terms of units of standard deviation. Although sometimes difficult to interpret, this analysis allows comparisons across numerous instruments measuring the same concept. Mishra et al. (2012) contains additional details on the data synthesis and analysis as well as subgroup analysis strategies.

Results

Trial Characteristics

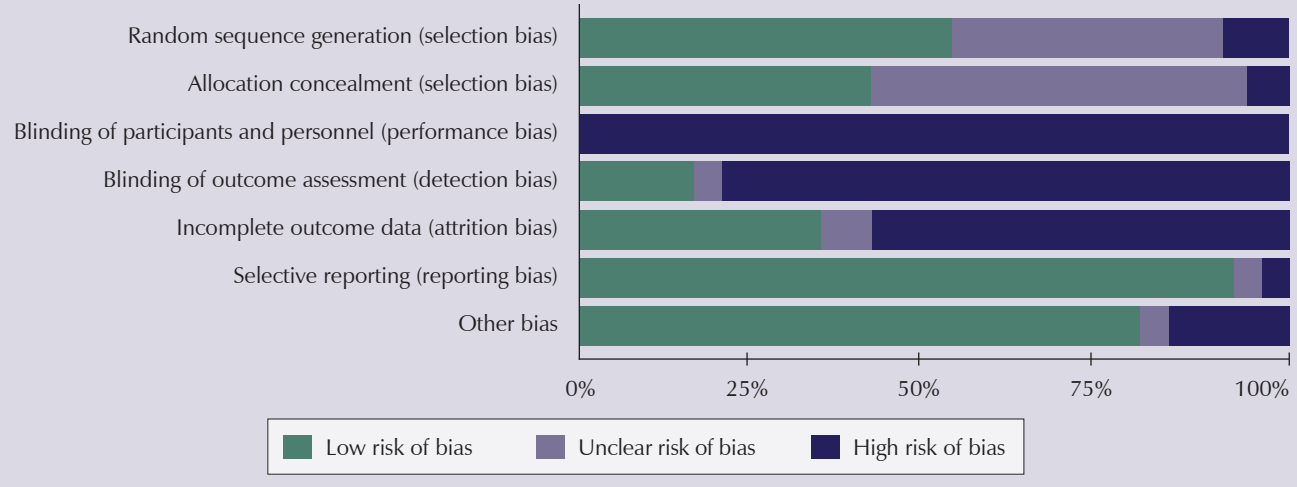
The search of electronic databases and other resources yielded 1,795 unduplicated citations. In all, 40 trials met the eligibility criteria and were included in the qualitative synthesis (see Appendix A) and, from these, 33 trials were included in a quantitative synthesis. Almost all trials (n = 38) were parallel RCTs, and two trials (Cho, Yoo, & Kim, 2006; Heim, Malsburg, & Niklas, 2007) used a quasi-randomized design to allocate participants to treatment. Thirty-six trials randomized eligible participants to either an exercise or comparison arm, and four trials included additional treatment arms comprised of variations in exercise, such as low- or moderate-intensity exercise (Burnham & Wilcox, 2002), exercise therapy or exercise placebo (Daley et al., 2007), exercise initiation during treatment or following treatment (Dodd et al., 2010); or exercise and exercise with behavioral modification (Segar et al., 1998). Mishra et al. (2012) contains additional details on trial characteristics (i.e., participants, interventions, outcome measures, and risk of bias).

Participants

Of the 3,694 participants randomized in each trial, 1,927 (range = 9–302) participants were randomized to the exercise and 1,764 (range = 7–271) participants to the comparison group. In one trial (Dimeo, Thomas, Raabe-Menssen, Propper, & Mathias, 2004), the number of participants randomized to the exercise and comparison arms did not add up to the number of participants randomized in the trial. The majority of trials investigated participants with breast cancer (n = 22) and an additional 12 trials investigated participants with a range of cancer diagnoses. The mean age of the participants ranged from 39–70 years, with one trial not reporting on the age of the participants (Berglund, Bolund, Gustafsson, & Sjoden, 1994). Thirty trials were conducted among participants who had completed active treatment for their cancer, and the remaining 10 trials included participants both during and after cancer treatment. One of these reported data separately on trial participants who completed treatment (Moadel et al., 2007) and only these data were included in the current review. Fewer than half of the trials reported on the past exercise history of the participants (n = 15).

Intervention

The exercise interventions differed across trials, with trials prescribing strength/resistance training, walking, cycling, yoga, Qigong, Tai Chi, or some combination. Thirty trials implemented an aerobic exercise program. Length of the exercise intervention varied greatly among trials, ranging from three weeks (Dimeo et al., 2004) to one year (Penttinen et al., 2011; Speck, Gross, et al., 2010) (modal duration = 12 weeks). Twenty-five trials assessed HRQOL or HRQOL domains immediately following the end of the interventions. Methods



Note. This graph represents the review authors' judgments about each risk of bias item presented as percentages across all included studies.

Figure 2. Risk of Bias

to measure exercise intensity varied and included subjective (i.e., mild, moderate, or vigorous) and objective (maximum heart rate, maximum oxygen consumption, perceived exertion, or the Borg scale) assessments. The duration of individual exercise sessions ranged from 20 minutes to greater than 90 minutes (modal duration = 30 minutes). Thirty trials were led by a professional (e.g., exercise physiologist, sports trainer, yoga instructor).

Risk of Bias Within Trials

The risk of bias in all trials was moderate to high. Given the nature of the intervention (exercise program), all trials were at a high risk for performance bias, in which systematic differences in outcomes measures are the result of knowing the intervention assigned to a study participant. The majority of trials were at a low risk for selection bias because of adequate generation of the randomization sequence and reporting bias and were at a high risk for detection and attrition bias (see Figure 2).

Effects of the Interventions

Tables 1 and 2 present findings on the effects of the exercise program on HRQOL or HRQOL domains. Various instruments were used to measure HRQOL or HRQOL domains in the included trials. (For a complete listing of these instruments, please contact the first author of this article.) These were grouped by domain for analyses. The authors have reported results as change from baseline or as follow-up scores. The authors conducted numerous meta-analyses, which need to be interpreted with caution given the fact that trials reported data on the outcomes using different types of assessment instruments and over varying follow-up periods.

Overall Health-Related Quality of Life

When measured as change in HRQOL score from baseline, HRQOL in study participants in the exercise group showed a significant improvement at 12 weeks and at 6 months compared with HRQOL in participants in the control group. However, no significant difference was noted between exercise and control groups at follow-up between 3 and 6 months. The authors also observed a significant improvement in HRQOL at 12 weeks when HRQOL was reported as scores at follow-up, but not at longer follow-up times. Two trials (Heim et al., 2007; Oh, Butow, Mullan, & Clarke, 2008) without quantitative data also reported that exercise resulted in an increase in HRQOL, although Heim et al. (2007) also reported an increase in HRQOL in the control group.

In subgroup analyses of the meta-analysis of HRQOL using change in HRQOL scores from baseline, a positive effect was observed of exercise for both breast (SMD 0.57; 95% CI [0.2, 0.95]) and all other cancers (SMD 0.27; 95% CI [0, 0.55]). Based on the authors' definition of exercise intensity, moderate-to-vigorous exercise resulted in a positive effect on HRQOL (SMD 0.29; 95% CI [0, 0.58]), but no effect was seen when the exercise was noted to be mild-to-moderate (SMD 0.46; 95% CI [–0.62, 1.53]). Similar patterns were observed when HRQOL was measured as values at follow-up rather than change from baseline. The authors did not conduct subgroups analyses at longer follow-up times because too few studies existed.

Domains of Health-Related Quality of Life

Findings for each HRQOL domain are summarized and presented in Table 1. Reported here are findings for domains that showed some consistency in effect across follow-up time periods or types of measures reported.

Anxiety: Anxiety was significantly reduced in the exercise group compared with the control group at 12 weeks, whether measured as change in scores from baseline or as follow-up scores. This reduction, however, was not observed at longer follow-up times. Subgroup analyses showed no significant effect on anxiety reduction at 12-weeks follow-up for breast cancer survivors (SMD –0.15; 95% CI [–0.61, 0.3]) or with vigorous-to-moderate exercise (SMD –0.26; 95% CI [–0.55, 0.03]). A significant effect was observed of mild-to-moderate exercise on anxiety (SMD –0.26; 95% CI [–0.02, –0.5]). Berglund et al. (1994), whose data could not be included in a meta-analysis, reported a reduction in anxiety in both exercise and control group, but no difference between groups.

Emotional well-being: When measured using change from baseline scores, exercise had a positive effect on emotional well-being at 12 weeks and 6 months follow-up time periods, but not between 3 and 6 months. Subgroup analyses showed that this significant effect was present in survivors with cancers other than breast cancer, but not survivors with breast cancer (SMD 0.43, 95% CI [0.16, 0.69] for all other versus SMD 0.3, 95% CI [–0.15, 0.75] for breast cancer). No significant difference was noted when subgroups were examined by reported exercise intensity. A positive effect of exercise was observed when emotional well-being was measured using scores at 12 weeks and between 3 and 6 months follow-up, but not follow-up scores at 6 months. The authors were not able to include data in a meta-analysis for one trial (Oh et al., 2008) that reported no change over time in emotional well-being in either the exercise or control group.

Fatigue: Pooling results of trials measuring change in fatigue from baseline showed a significant decrease in fatigue following exercise compared with the control intervention at 12 weeks and between 3 and 6 months, but not at 6 months. Trials measuring scores in fatigue scales at follow-up also showed a positive effect of

Table 1. Standardized or Weighted Mean Differences and 95% Confidence Interval (CI) Between Control and Exercise Group for Health-Related Quality of Life (HRQOL) and Its Domains by Time Point

	Change in Scores From Baseline to 12 Weeks		Scores at 12 Weeks		Change in Scores From Baseline to > 12 Weeks and Up to 6 Months		Scores at > 12 Weeks Up to 6 Months		Change in Scores From Baseline to 6 Months		Scores at 6 Months	
Domain	**$\bar{X}$**	**95% CI**	**$\bar{X}$**	**95% CI**	**$\bar{X}$**	**95% CI**	**$\bar{X}$**	**95% CI**	**$\bar{X}$**	**95% CI**	**$\bar{X}$**	**95% CI**
HRQOL	**0.48**	**[0.16, 0.81]**	**0.49**	**[0.24, 0.74]**	0.14	[–0.38, 0.66]	0.11	[–0.1, 0.32]	**0.46**	**[0.09, 0.84]**	0.25	[–0.12, –0.62]
Anxiety	**–0.26**	**[–0.44, –0.07]**	**–0.4**	**[–0.77, –0.03]**	0.06	[–0.23, 0.35]	0.13	[–0.15, 0.42]	–0.15	[–0.61, 0.3]	–0.14	[–0.6, 0.31]
Breast cancer concerns	–0.13	[–0.41, 0.14]	**2.2**[a]	**[0.69, 3.72]**	**0.99**	**[0.41, 1.57]**	1.81[a]	[–0.35, 3.98]	0.14	[–0.24, 0.51]	2.05[a]	[–0.2, 4.3]
Body image	–1.09	[–2.29, 0.11]	–0.5	[–0.79, –0.2]	**–0.74**	**[–1.3, –0.18]**	–0.31	[–0.83, 0.2]	–0.05	[–0.51, 0.4]	–0.2	[–0.65, 0.26]
Cognitive functioning	–0.06	[–0.38, 0.26]	0.29	[–0.57, 1.16]	–	–	–0.26	[–0.55, 0.03]	–0.23	[–0.89, 0.43]	–	–
Depression	–0.13	[–0.51, 0.24]	**–0.41**	**[–0.65, –0.17]**	0.04	[–0.25, 0.33]	–0.1	[–0.41, 0.2]	–0.22	[–0.68, 0.24]	0.12	[–0.33, 0.58]
Emotional well-being	**0.33**	**[0.05, 0.61]**	**0.24**	**[0.12, 0.37]**	0.13	[–0.34, 0.6]	**0.17**	**[0.01, 0.32]**	**0.6**	**[0.17, 1.03]**	0.13	[–0.16, 0.41]
Fatigue	**–0.82**	**[–1.5, –0.14]**	**–0.3**	**[–0.46, –0.14]**	**–0.42**	**[–0.83, –0.02]**	–0.03	[–0.31, 0.25]	–0.06	[–0.31, 0.19]	–0.1	[–0.48, 0.27]
General health perspective	0.11	[–0.29, 0.51]	0.14	[–0.2, 0.49]	–	–	0.19	[–0.19, 0.58]	0.03	[–0.38, 0.44]	0.03	[–0.3, 0.36]
Pain	0.09	[–0.43, 0.61]	**–0.29**	**[–0.55, –0.04]**	–	–	0.05	[–0.34, 0.43]	0.22	[–0.24, 0.68]	0.05	[–0.4, 0.51]
Physical function	0.29	[–0.08, 0.66]	**0.36**	**[0.09, 0.64]**	0.28	[–0.28, 0.85]	0.25	[–0.05, 0.54]	–0.11	[–0.69, 0.48]	0.19	[–0.18, 0.57]
Role function	0.15	[–0.16, 0.46]	**0.27**	**[0.04, 0.5]**	0.18	[–0.37,0.73]	0.18	[–0.06, 0.42]	0.07	[–0.22, 0.35]	0.16	[–0.13, 0.44]
Sexuality	–	–	0.28	[–0.11, 0.68]	–	–	–	–	**0.4**	**[0.11, 0.68]**	0.21	[–0.07, 0.49]
Sleep disturbance	0.1	[–0.3, 0.5]	**–0.46**	**[–0.72, 0.2]**	–	–	–0.52	[–1.64, 0.61]	–	–	–	–
Social function	**0.45**	**[0.02, 0.87]**	0.23	[–0.02, 0.48]	0.37	[–0.18, 0.92]	0.08	[–0.16, 0.31]	**0.49**	**[0.11, 0.87]**	0.33	[–0.04, 0.71]
Spirituality	0.05	[–2.89, 2.99]	1.51[a]	[–3.64, 6.65]	–	–	–	–	–	–	–	–

[a] Weighted mean differences. All other values are standardized mean differences.

Note. Values are reported as a change in score on HRQOL from baseline to follow-up or as scores recorded on HRQOL forms at follow-up visit. Positive values indicate an improvement in HRQOL or its domains except for anxiety, body image, cognitive function, depression, pain, and sleep disturbance. In these cases a negative value indicates an improvement in HRQOL domain.

Note. Significant findings are bolded. If no data were provided for a time point, the cell contains a dash.

exercise on fatigue, but only at 12 weeks follow-up. No treatment difference was noted by subgroups of cancer type (breast cancer: SMD –0.28, 95% CI [–0.77, 0.2] versus other types of cancer: SMD –1.47, 95% CI [–3.12, 0.19]), or exercise intensity (moderate-to-vigorous SMD –1.35, 95% CI [–3.08, 0.38] versus mild-to-moderate SMD –0.51, 95% CI [–1.27, 0.25]). Three of four trials without quantitative data reported no group differences in fatigue (Dodd et al., 2010; Oh et al., 2008; Payne, Held, Thorpe, & Shaw, 2008); the remaining trial (Heim et al., 2007) reported improvement in both treatment groups and continued improvement in the exercise group over time compared with increased fatigue in the control group.

Other domains: Table 1 shows additional HRQOL domains that showed a significant effect of exercise compared with a control intervention, although these should be interpreted with caution as isolated findings may be spurious. Because the authors completed multiple comparisons, some findings may show significance by chance. An observed significant effect of exercise on social function was noted at 12 weeks and at 6 months

Table 2. Overall Health-Related Quality of Life (HRQOL) Change Score at Follow-Up

	Exercise			Control			Weight	Standard $\bar{X}$ Difference
Study or Subgroup	$\bar{X}$	SD	Total	$\bar{X}$	SD	Total	(%)	IV, Random, 95% CI
1.1.1 Up to 12 Weeks[a]								
Cadmus et al., 2009	0.3	5.7	37	0.2	4.4	37	9.9	0.02 [–0.44, 0.48]
Cho et al., 2006	0.9	1.3	28	–0.1	1	27	9	0.85 [0.29, 1.4]
Courneya et al., 2009	10.6	22.1	60	1.1	22.1	62	10.7	0.43 [0.07, 0.79]
Dimeo et al., 2004	17	51	62	20	36	17	9.2	–0.06 [–0.6, 0.48]
Herrero et al., 2006	17.7	8.3	8	–10.4	17.7	8	4.3	1.92 [0.68, 3.17]
McNeely et al., 2008	4.4	10.6	27	1.7	6.9	25	9.1	0.29 [–0.25, 0.84]
Mehnert et al., 2011	9.72	21.03	30	5.55	16.5	27	9.3	0.22 [–0.31, 0.74]
Milne et al., 2008	12.6	12.6	29	–3	8	29	8.8	1.46 [0.87, 2.04]
Oh et al., 2010	8.86	9	54	–0.13	8.6	54	10.3	1.01 [0.61, 1.42]
Rogers et al., 2009	4.5	8.4	20	2.9	12	18	8.3	0.15 [–0.49, 0.79]
Targ & Levine, 2002	4.98	16.1	79	6.62	21.7	88	11.1	–0.08 [–0.39, 0.22]
Subtotal	–	–	434	–	–	392	100	0.48 [0.16, 0.81]
1.1.2 More Than 12 Weeks to Less Than 6 Months[b]								
Courneya, Friedenreich, Sela, et al., 2003	0.9	12.2	62	2	9	31	38.7	–0.1 [–0.53, 0.33]
Courneya, Mackey, et al., 2003	5.7	7.4	24	0.6	7.4	28	32.6	0.68 [0.12, 1.24]
Thorsen et al., 2005	8.8	9.4	18	10.4	9.7	18	28.7	–0.16 [–0.82, 0.49]
Subtotal	–	–	104	–	–	77	100	0.14 [–0.38, 0.66]
1.1.3 6 Months[c]								
Ohira et al., 2006	2.3	4.5	39	0.6	4	40	69.4	0.4 [–0.05, 0.84]
Rogers et al., 2009	3.4	11	19	–3.5	10.8	17	30.6	0.62 [–0.05, 1.29]
Subtotal	–	–	58	–	–	57	100	0.46 [0.09, 0.84]

[a] Heterogeneity tau^2 = 0.22; chi^2 = 46.35, df = 10 ($p < 0.00001$); I^2 = 78%. Test for overall effect: Z = 2.95 (p = 0.003)
[b] Heterogeneity tau^2 = 0.13; chi^2 = 5.49, df = 2 (p = 0.06); I^2 = 64%. Test for overall effect: Z = 0.52 (p = 0.61)
[c] Heterogeneity tau^2 = 0.00; chi^2 = 0.29, df = 1 (p = 0.59); I^2 = 0%. Test for overall effect: Z = 2.45 (p = 0.01)
CI—confidence interval
Note. Test for subgroup differences: chi^2 = 1.34, df = 2 (p = 0.51), I^2 = 0%

when looking at the change from baseline to follow-up scores, but not when looking at the follow-up scores. In addition, significant findings for body image and breast cancer concerns were observed when looking at follow-up scores at 12 weeks and at change in score from baseline to follow-up between 12 weeks and 6 months. In addition, significant effects on depression, pain, physical function, role function, sexuality, and sleep disturbance were seen at a single point in time and using a single type of measure.

Discussion

Findings from this review indicate that exercise interventions have a positive impact on overall HRQOL and certain HRQOL domains, including anxiety, emotional well-being, fatigue, and social functioning. The positive effects were consistent either across time frame or when observed, as measured by change from baseline or follow-up scores, or both.

Some of the evidence on the effectiveness of exercise intervention on HRQOL or HRQOL domains reported in this article finds support in the literature. However, caution should be exercised when comparing findings with other reviews because other reviews included people both during and after cancer treatment. Similar to other reviews, the authors documented positive effects of exercise interventions on overall HRQOL (Ferrer, Huedo-Medina, Johnson, Ryan, & Pescatello, 2011; Speck, Courneya, Masse, Duval, & Schmitz, 2010) and fatigue (Cramp & Byron-Daniel, 2012). Unlike findings reported by Cramp, James, and Lambert (2010), the authors observed lower anxiety among people in exercise programs. In addition, in contrast with findings reported by Duijts, Faber, Oldenburg, van Beurden, and Aaronson (2011), the authors of the current study observed positive trends for HRQOL domains of depression and body image. Variations in findings reported by the reviews could be explained by differences in inclusion criteria, treatment status, duration of the exercise intervention, and measures used to assess HRQOL and HRQOL domain outcomes.

Implications for Research

Several areas for future research can improve understanding of the effects of exercise on HRQOL. Most of the current research is atheoretical and could benefit from conceptual models that are ecologic-based (Glanz, Rimer, & Viswanath, 2008) to further clarify individual, social, structural, and policy environments conducive for behavior change. In addition, the conceptual models could help guide the design and implementation of exercise interventions, assessment of patient-reported outcomes, and appropriate statistical plans. There also is a need to understand the necessary intensity, frequency, duration, and format of exercise programs for optimal and sustainable effect. The heterogeneity of measures used to assess HRQOL and its domains could be addressed by efforts such as the Patient-Reported Outcomes Measurement Information System (PROMIS) (Cella et al., 2010; National Cancer Institute, 2014). All trials reviewed had a common limitation: failure to recreate the context within which the intervention was delivered and changes in behavior occurred. This limitation could be addressed by using mixed methods research designs (Creswell, 2014) to gain contextually meaningful insights about the exercise program and patient-reported outcomes. Lastly, given the growing body of literature attesting to the beneficial effects of exercise on HRQOL or its domains, a need exists to identify effective strategies for the dissemination and implementation (Brownson, Colditz, & Proctor, 2012) of this evidence into practice and policy.

Caution needs to be applied when interpreting the positive results. The trials included in the review had various degrees of bias. A wide variation existed in the exercise programs and outcomes measurement instruments. Although the authors used rigorous methodologies (Mishra et al., 2012) for the search strategy, inclusion of eligible trials, and data abstraction methodology, some literature may have been missed. Funnel plots (Mishra et al., 2012) reveal minor asymmetry indicating only slight publication bias. In addition, because the authors had multiple comparisons, some findings may be significant by chance. The authors also compared finding by domain across time periods and across metrics (i.e., change from baseline versus follow-up scores). Consistent findings across these measures suggest a more robust finding and increases confidence in the significance of a given result.

As with any systematic review and meta-analysis, it was a challenge to address the lack of consistency in reporting, both related to general study considerations

Knowledge Translation

Cancer survivors who have completed primary treatment can benefit from exercise programs, which have beneficial efforts on overall health-related quality of life (HRQOL).

Exercise programs also have positive effects on HRQOL domains as they can enhance social functioning and emotional well-being and reduce anxiety and fatigue.

Moderate-to-vigorous exercise has positive effects on overall HRQOL. Exercise programs can include strength or resistance training, walking, cycling, yoga, Qigong, tai chi, or some combination.

and to HRQOL outcomes in particular. The Consolidated Standards of Reporting Trials (CONSORT) statement has provided general guidance for the publication of RCTs since 1996, with its most recent update in 2010 (Schulz, Altman, & Moher, 2010). Guidelines addressing the specific reporting considerations for HRQOL and other patient-reported outcomes have been published (Brundage et al., 2013), including a CONSORT extension (Calvert et al., 2013). Future literature syntheses will be aided if authors and journals implement these guidelines for patient-reported outcomes.

Implications for Practice

This review identified several beneficial effects of exercise interventions on HRQOL and its domains. In addition, as evidence accumulates, research will become increasingly precise in identifying what kinds of exercise interventions benefit which cancer survivors. In the meantime, the current evidence supports the translation of the accumulated knowledge base to practice. The evidence reported in this article should help inform healthcare professionals, cancer survivors, educators, and policy makers that exercise programs have a beneficial effect on HRQOL and its domains, and that exercise programs should be integrated into the management plans of cancer survivors who have completed treatment.

Conclusion

Evidence presented in this review indicates that exercise programs have a beneficial effect on HRQOL and its domains and can be integrated into the management plans for cancer survivors who have completed treatment. In addition, the evidence presented supports the inclusion of exercise programs for the management of cancer survivors who have completed treatment into clinical guidelines, such as the Oncology Nursing Society's Putting Evidence Into Practice resource.

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Appendix A. Characteristics of Participants and Interventions in Reviewed Trials

Study	Sample	Size	Time After Treatment	Exercise Program	Intervention and Follow-Up	Intensity and Duration	Format, Location, and Supervision
Bai et al., 2004	Men and women with cancer of the nasopharynx with no prior exercise	45 total participants; 24 in the exercise group and 21 in the control group	Immediate	Jogging, swimming, and exercise with equipment; relaxation training of body muscles; education on diseases and psychological support	The intervention lasted for three months, with follow-up conducted to the end of the intervention period.	Low to moderate; duration not reported	Individual format; location and whether there was supervision was not reported
Banasik et al., 2011	Women with breast cancer with no prior exercise	18 total participants; 9 in the exercise group and 9 in the control group	At least two months	Iyengar yoga	The intervention lasted eight weeks, with follow-up conducted to the end of the intervention period.	Mild; 90 minutes	Group format in a facility with professional supervision
Berglund et al., 1994	Participants with various cancers and no prior exercise	199 total participants; 98 in the exercise group and 101 in the control group	Not reported	Physical training (exercises to increase mobility, muscle strength, general fitness, and relaxation of body muscles), information, and coping skills training	The intervention lasted seven weeks, with follow-up conducted at 12 months	Not reported	Group format in a facility with professional supervision
Bourke et al., 2011	Men and women with colorectal cancer and no prior exercise	18 total participants; 9 in the exercise group and 9 in the control group	16.4 mean months for the exercise group and 16.7 for the control group	Exercise using treadmills, rowing ergometers, and cycling ergometers; resistance exercises; and dietary advice	The intervention lasted 12 weeks, with follow-up conducted to the end of the intervention period.	55%–85% of age predicted max heart rate (HR); duration was 30 minutes or longer	Group and individual formats, both in a facility and in the home, with professional supervision available
Burnham & Wilcox, 2002	Men and women with various cancers and no prior exercise	21 total participants; 14 in the exercise group and 7 in the control group	10.3 mean months (SD = 5.1) for low-intensity exercise; 9.8 (SD = 4.2) for moderate-intensity exercise; and 9 (SD = 5.3) for controls	Exercise (not specified)	The intervention lasted 10 weeks, with follow-up conducted to the end of the intervention period.	Low (25%–35% of HR reserve) to moderate (40%–50% of HR reserve) with various duration	Group format in a facility; use of professional supervision was unclear
Cadmus et al., 2009	Women with breast cancer who had previously exercised	75 total participants; 37 in the exercise group and 38 in the control group	At least 12 months	Exercise (not specified)	The intervention lasted six months, with follow-up conducted to the end of the intervention period.	60%–80% of predicted max HR; duration was 30 minutes	Individual format both in a facility and at home, with professional supervision

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Appendix A. Characteristics of Participants and Interventions in Reviewed Trials *(Continued)*

Study	Sample	Size	Time After Treatment	Exercise Program	Intervention and Follow-Up	Intensity and Duration	Format, Location, and Supervision
Cho et al., 2006	Women with breast cancer with no prior exercise	65 total participants; 34 in the exercise group and 31 in the control group	15.5 mean months (SD = 5.9) for the exercise group and 17 (SD = 6.2) for the control group	Exercise (not specified), psychology-based education, and peer support group activity	The intervention lasted 10 weeks, with follow-up conducted to the end of the intervention period.	40%–60% of max HR; duration was 90 minutes	Group and individual format in both a facility and at home, with professional supervision available
Cohen et al., 2004	Men and women with lymphoma who had previously exercised	39 total participants; 20 in the exercise group and 19 in the control group	Not reported	Tibetan yoga exercise, including controlled breathing and visualization, mindfulness, postures from the Tsa lung, and Trul khor (sngon 'gro)	The intervention lasted seven weeks, with follow-up conducted to the end of the intervention period.	Mild intensity with duration not reported	Group and individual format in both a facility and at home, with professional supervision available
Courneya et al., 2009	Men and women with lymphoma who had previously exercised	122 total participants; 60 in the exercise group and 62 in the control group	Not reported	Upright or recumbent cycle ergometer, interval training above the ventilatory threshold in week 7, VO_2 peak interval training in week 9	The intervention lasted 12 weeks, with follow-up occurring 6 months after end of the intervention.	60%–75% of peak power output (VO_2 peak); duration varied	Group format in a facility with professional supervision
Courneya, Friedenreich, Quinney, et al., 2003	Men and women with colorectal cancer who had previously exercised	102 total participants; 69 in the exercise group and 33 in the control group	Within the previous three months	Personalized exercise program, including any activity designed to improve functional well-being through cardiovascular and flexibility exercises. If none, walking was prescribed	The intervention lasted 16 weeks, with follow-up conducted to the end of the intervention period.	65%–75% of estimated max HR; duration was 20–30 minutes	Individual format at home with no professional supervision
Courneya, Friedenreich, Sela, et al., 2003	Men and women with various cancers who had previously exercised	108 total participants; 60 in the exercise group and 48 in the control group	Not reported	Personalized exercise program including walking or choice of alternate mode of exercise (e.g., swimming, cycling); group psychotherapy	The intervention lasted 10 weeks, with follow-up conducted to the end of the intervention period.	65%–75% of estimated max HR; duration was 20–30 minutes	Individual format in both a facility and at home with no professional supervision
Courneya, Mackey, et al., 2003	Women with breast cancer who had previously exercised	53 total participants; 25 in the exercise group and 28 in the control group	Not reported	Recumbent or upright cycle ergometer	The intervention lasted 15 weeks, with follow-up conducted to the end of the intervention period.	70%–75% of max oxygen consumption; duration varied	Format was unclear, but the intervention took place in a facility with professional supervision

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Appendix A. Characteristics of Participants and Interventions in Reviewed Trials *(Continued)*

Study	Sample	Size	Time After Treatment	Exercise Program	Intervention and Follow-Up	Intensity and Duration	Format, Location, and Supervision
Culos-Reed et al., 2006	Men and women with various cancers and no prior exercise	38 total participants; 20 in the exercise group and 18 in the control group	More than three months	Yoga	The intervention lasted seven weeks, with follow-up conducted to the end of the intervention period.	Intensity was unclear; duration was 75 minutes	Group format in a facility with professional supervision
Daley et al., 2007	Women with breast cancer who had previously exercised	108 total participants; 34 in the exercise group and 74 in the control group	12–36 months	Exercise sessions (not specified) with specialist; exercise education/guidance	The intervention lasted eight weeks, with follow-up occurring 24 weeks postintervention.	65%–85% of age-adjusted max HR; duration was 50 minutes	Individual format in a facility with professional supervision
Danhauer et al., 2009	Women with breast cancer who had previously exercised	44 total participants; 22 in the exercise group and 22 in the control group	2–24 months after primary treatment	Restorative yoga which combined physical postures (asanas), breathing (pranayama), and deep relaxation (savasana). Poses included: mountain pose, arm and shoulder stretch, supported forward fold, seated sun salutation, and reclining twist with a bolster	The intervention lasted 10 weeks, with follow-up conducted to the end of the intervention period.	Mild intensity; duration was 75 minutes	Group format in a facility with professional supervision
Dimeo et al., 2004	Men and women with various cancer and no prior exercise	69 total participants randomized; with 34 in the exercise group and 35 in the control group	126 mean days (SD = 153) in the exercise group and 134 (SD = 151) in the control group	Stationary biking	The intervention lasted three weeks, with follow-up conducted to the end of the intervention period.	80% of max HR; duration was 30 minutes	Group format in a facility, but whether professional supervision was available is unclear
Dodd et al., 2010	Women with various cancer who had previously exercised	119 total participants; 80 in the exercise group and 39 in the control group	Not reported	Individualized program adjusted to participant's fitness level and adjusted weekly to maintain the exercise prescription, which consisted of a cardiovascular/aerobic exercise (e.g. walking, jogging, cycling)	The intervention lasted 4–6 months with follow-up occurring 6–8 months postintervention.	60%–80% VO_2 peak; duration varied	Individual format in the home with professional supervision
Donnelly et al., 2011	Women with various cancer and no prior exercise	33 total participants; 16 in the exercise group and 17 in the control group	Not reported	Physical activity, including walking and strengthening exercises	The intervention lasted 12 weeks, with follow-up occurring six months postintervention.	Moderate intensity; duration was 30 minutes	Individual format in the home with professional supervision

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Appendix A. Characteristics of Participants and Interventions in Reviewed Trials *(Continued)*

Study	Sample	Size	Time After Treatment	Exercise Program	Intervention and Follow-Up	Intensity and Duration	Format, Location, and Supervision
Fillion et al., 2008	Women with breast cancer with no prior exercise	94 total participants; 48 in the exercise group and 46 in the control group	Two years or less	Walking training, walking, psychoeducative, and fatigue management	The intervention lasted four weeks, with follow-up occurring three months post-intervention.	Intensity was unclear; duration was 60 minutes	Group format, in both a facility and at home, with professional supervision
Heim et al., 2007	Women with breast cancer who had previously exercised	63 total participants; 32 in the exercise group and 31 in the control group	Not reported	Educational program, physical therapy, group exercise, and psycho-oncologic interventions; brochure with instructions for muscle strength and stretching exercises; instructions for aerobic exercises (walking program), coordination, and relaxation	The intervention length was unclear, but follow-up occurred three months postintervention.	Not reported	Individual format in a facility or at home with professional supervision
Herrero et al., 2006	Women with breast cancer who had no prior exercise	20 total participants; 10 in the exercise group and 10 in the control group	36 mean months (SD = 13) for the exercise group and 35 (SD = 12) for control	Cycle-ergometer pedaling, stretching exercises, and resistance training	The intervention lasted eight weeks, with follow-up conducted to the end of the intervention period.	Intensity was not reported, but duration was 90 minutes	Format was unclear, but intervention took place in a facility with professional supervision
Knols et al., 2011	Men and women with various cancer who had previously exercised	131 total participants; 64 in the exercise group and 67 in the control group	81 mean days (SD = 36) for the exercise group and 78 (SD = 35) for the control group	Endurance exercises (including ergometer cycling), progressive resistance training, and a standard strength program	The intervention lasted 12 weeks, with follow-up occurring three months postintervention.	Intensity varied; duration was 30 minutes	Format was unclear, but intervention took place in a facility with professional supervision
McNeely et al., 2008	Men and women with head and neck cancer who had previously exercised	52 total participants; 27 in the exercise group and 25 in the control group	12 months (range = 2–120) for the exercise group and 17 (range = 2–180) for the control group	Progressive resistance exercise training consisting of active and passive range of motion/stretching exercises, postural exercises, basic strengthening exercises, and tailored strengthening exercises	The intervention lasted 12 weeks, with follow-up conducted to the end of the intervention period.	Intensity varied; duration was unclear	Format was unclear, but intervention took place in a facility and home with professional supervision
Mehnert et al., 2011	Women with breast cancer who had previously exercised	63 total participants; 35 in the exercise group and 28 in the control group	At least four weeks	Physical training program including gymnastics, movement games, relaxation, moderate walking, and jogging	The intervention lasted 10 weeks, with follow-up conducted to the end of the intervention period.	Max of 60% of VO_2; duration was 90 minutes	Group format in a facility with professional supervision

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Appendix A. Characteristics of Participants and Interventions in Reviewed Trials *(Continued)*

Study	Sample	Size	Time After Treatment	Exercise Program	Intervention and Follow-Up	Intensity and Duration	Format, Location, and Supervision
Milne et al., 2008	Women with breast cancer with no prior exercise	58 total participants; 29 in the exercise group and 29 in the control group	12.6 mean months (SD = 4.62) for the exercise group and 13.4 (SD = 3.4) for control	Combined aerobic (cycle and rowing ergometers, mini-trampoline, and step-up blocks), resistance training, and stretching	The intervention lasted 12 weeks, with follow-up conducted to the end of the intervention period.	Intensity varied; duration was 60 minutes	Group and individual format in a facility with professional supervision
Moadel et al., 2007	Women with breast cancer with no prior exercise	164 total participants; 108 in the exercise group and 56 in the control group	Not reported	Yoga, which combined physical stretches and poses, breathing exercises, and meditation	The intervention lasted 12 weeks, with follow-up conducted to the end of the intervention period.	Mild intensity; duration was 90 minutes	Group and individual format in a facility and at home with professional supervision
Mustian et al., 2004	Women with breast cancer with no prior exercise	31 total participants; 17 in the exercise group and 14 in the control group	1 week to 30 months	Tai Chi Chuan, which combined warm-up exercises and basic Chi Kung, Tai Chi Chuan, short-form of Yang-style Tai Chi Chuan, regulatory breathing, imagery, and meditation	The intervention lasted 12 weeks, with follow-up conducted to the end of the intervention period.	Moderate intensity; duration was 60 minutes	Group format in a facility with professional supervision
Oh et al., 2008	Men and women with various cancers and no prior exercise	30 total participants; 15 in the exercise group and 15 in the control group	Not reported	Medical Qigong, which combined general discussion, gentle stretching and body movement in standing and seated postures, and breathing exercise	The intervention lasted eight weeks, with follow-up conducted to the end of the intervention period.	Mild intensity; duration varied	Group and individual format in a facility and at home with professional supervision
Oh et al., 2010	Men and women with various cancers and no prior exercise	162 total participants; 79 in the exercise group and 83 in the control group	Not reported	Medical Qigong, which combined general discussion, gentle stretching and body movement in standing and seated postures, meditation, and breathing exercises	The intervention lasted 10 weeks, with follow-up conducted to the end of the intervention period.	Mild intensity; duration varied	Group and individual format in a facility and at home with professional supervision
Ohira et al., 2006	Women with breast cancer with no prior exercise	86 total participants; 43 in the exercise group and 43 in the control group	1.21 mean years (range = 0.28–2.84) for the exercise group and 2.02 (range = 0.44–11.42) for the control group	Weight training and stretching exercises	The intervention lasted six months, with follow-up conducted to the end of the intervention period.	Not reported	Group and individual format in a facility with professional supervision

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Appendix A. Characteristics of Participants and Interventions in Reviewed Trials *(Continued)*

Study	Sample	Size	Time After Treatment	Exercise Program	Intervention and Follow-Up	Intensity and Duration	Format, Location, and Supervision
Payne et al., 2008	Women with breast cancer and no prior exercise	20 total participants; 10 in the exercise group and 10 in the control group	Not reported	Walking activity	The intervention lasted 14 weeks, with follow-up conducted to the end of the intervention period.	Moderate intensity; duration was 20 min	Individual format in the home with no professional supervision
Penttinen et al., 2011	Women with breast cancer who had previously exercised	573 total participants; 302 in the exercise group and 271 in the control group	Median weeks from surgery, 33; chemotherapy, 12; last radiation, 4	Two components which were performed in alternate weeks and included vigorous step aerobics and circuit training	The intervention lasted 12 months, with follow-up conducted to the end of the intervention period.	Vigorous intensity; duration was 60 minutes	Group and individual format in a facility and at home with professional supervision
Pinto et al., 2003	Women with breast cancer with no prior exercise	24 total participants; 12 in the exercise group and 12 in the control group	323 mean days (SD = 212.3)	Cardiovascular activity, strength (weight) training, and flexibility	The intervention lasted 12 weeks, with follow-up occurring within one week postintervention.	60%–70% of peak HR; duration was 50 minutes	Group and individual format in a facility and at home with professional supervision
Pinto et al., 2005	Women with breast cancer with no prior exercise	86 total participants; 43 in the exercise group and 434 in the control group	Not reported	Physical activity program, including brisk walking, biking, swimming, or use of home exercise equipment; instruction on exercising; physical activity counseling, including individually based reinforcement, problem-solving, and monitoring participation; tip sheets on physical activity; and cancer survivorship tip sheet	The intervention lasted 12 weeks, with follow-up occurring at 12 weeks, six months, and nine months postintervention.	55%–65% of max HR; duration varied	Individual format at home; whether professional supervision was available is unclear
Rogers et al., 2009	Women with breast cancer with no prior exercise	41 total participants; 21 in the exercise group and 20 in the control group	Mean months for exercise: surgery, 35; chemotherapy, 36; and radiation, 35; and for control: surgery, 34; chemotherapy, 30; and radiation: 30	Exercise program (walking), discussion sessions, and update counseling sessions	The intervention lasted 12 weeks, with follow-up occurring three months postintervention.	Varied intensity; duration not reported	Group and individual format in a facility and at home, with professional supervision

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Appendix A. Characteristics of Participants and Interventions in Reviewed Trials *(Continued)*

Study	Sample	Size	Time After Treatment	Exercise Program	Intervention and Follow-Up	Intensity and Duration	Format, Location, and Supervision
Segar et al., 1998	Women with breast cancer with no prior exercise	30 total participants; 20 in the exercise group and 10 in the control group	Mean months for the exercise group was 43.7 (SD = 26.2) and, for the control group, was 38.1 (SD = 23.2)	Exercise with stationary bike, stair climbers, and hydraulic resistance exercise equipment, with type of exercise chosen by participant	The intervention lasted 10 weeks, with follow-up occurring 12 weeks postintervention.	60% or greater of predicted max HR; duration varied	Format was unclear; although it did take place in a facility, professional supervision was unclear as well
Speck, Gross, et al., 2010	Women with breast cancer and no prior exercise	295 total participants; 148 in the exercise group and 147 in the control group	Not reported	Progressive strength (weight) training including cardiovascular exercise warm-up, brief range of motion stretching, and strength training	The intervention lasted 12 months, with follow-up conducted to the end of the intervention period.	Intensity was not reported; duration was 90 minutes	Group format in a facility with professional supervision
Tang et al., 2010	Men and women with various cancers with no prior exercise	72 total participants; 37 in the exercise group and 35 in the control group	Not reported	Walking exercise and exercise booklet	The intervention lasted eight weeks, with follow-up occurring one and two months postintervention.	Rating of perceived exertion; duration was 40 minutes	Individual format, at home, with no professional supervision
Targ & Levine, 2002	Women with breast cancer who had previously exercised	181 total participants; 93 in the exercise group and 88 in the control group	Not reported	Intensive lifestyle change and group support program that included: Health series discussion group, dance/movement program, and silent meditation and guided imagery	The intervention lasted 12 months, with follow-up conducted to the end of the intervention period.	Mild to moderate intensity; duration was 90 minutes	Group format in a facility with professional supervision
Thorsen et al., 2005	Men and women with various cancers and no prior exercise	139 total participants; 69 in the exercise group and 70 in the control group	28 mean days (SD = 9)	Exercise program that included walking, cycling, jogging, and ball games	The intervention lasted 14 weeks, with follow-up conducted to the end of the intervention period.	60%–70% of max HR; duration was 30 minutes	Individual format, at home, with professional supervision