Published OnlineFirst November 4, 2010; DOI: 10.1158/1055-9965.EPI-10-0988

Cancer Epidemiology, Biomarkers & Prevention

Research Article

Efficacy of Exercise Interventions in Modulating Cancer-Related Fatigue among Adult Cancer Survivors: A Meta-Analysis

Justin C. Brown[1], Tania B. Huedo-Medina[1], Linda S. Pescatello[1], Shannon M. Pescatello[2], Rebecca A. Ferrer[3], and Blair T. Johnson[1]

Abstract

Background: The purpose of this meta-analysis was to explore the efficacy of exercise as a nonpharmacologic intervention to reduce cancer-related fatigue (CRF) among adult cancer survivors. We also investigated how different components of the exercise prescription (Ex R_x), methodologic considerations, and subject characteristics modulate CRF.

Methods: A systematic search for randomized controlled trials was conducted using words related to cancer, exercise, and fatigue.

Results: In total, 44 studies with 48 interventions qualified, including 3,254 participants of varying cancer types, stages of diagnosis, treatments, and exercise interventions. Cancer survivors in exercise interventions reduced their CRF levels to a greater extent than usual care controls, $d_+ = 0.31$ (95% CI = 0.22–0.40), an effect that appeared to generalize across several types of cancer. CRF levels improved in direct proportion to the intensity of resistance exercise ($\beta = 0.60$, $P = 0.01$), a pattern that was stronger in higher quality studies ($\beta = 0.23$, $P < 0.05$). CRF levels also reduced to a greater extent when interventions were theoretically driven ($\beta = 0.48$, $P < 0.001$) or cancer survivors were older ($\beta = 0.24$, $P = 0.04$).

Conclusions: Exercise reduced CRF especially in programs that involved moderate-intensity, resistance exercise among older cancer survivors and that were guided by theory.

Impact: Our results indicate exercise interventions for adult cancer survivors should be multi-dimensional and individualized according to health outcome and cancer type. *Cancer Epidemiol Biomarkers Prev; 20(1); 123–33.* *©2011 AACR.*

Introduction

Currently, there are over 11 million cancer survivors in the United States (1). The 5-year survival rate for cancer survivors has steadily increased from 50% in 1974 to 66% in 2004 (1). Despite living longer after diagnosis, cancer survivors commonly report having 1 or more cancer-related symptoms that impact their quality of life and activities of daily living (e.g., 2). One of the most commonly reported symptoms by cancer survivors is cancer-related fatigue (CRF; ref. 3). CRF is a reported side effect of all types of cancer treatment (4) affecting nearly 100% of cancer survivors and persists for years after treatment cessation (5, 6). Cancer survivors often state that CRF is the most distressing symptom related to cancer or cancer treatment, more so than pain, nausea, and vomiting (2, 7, 8).

Cancer survivors often are told by medical providers to learn to live with CRF by limiting activity, conserving energy expenditure, and relying on others to complete activities of daily living (3). Yet, new evidence is accumulating that indicates cancer survivors who engage in exercise experience numerous physical and mental health benefits including increased functional capacity (4), improved quality of life (9), and diminished depression and anxiety (10). In addition, meta-analyses (11–14) and systematic reviews (15) suggest that exercise interventions may be moderately efficacious in modulating CRF.

Despite the promise of exercise in the management of CRF, an exercise prescription (Ex R_x) tailored for adult cancer survivors experiencing CRF does not exist (3, 4, 16, 17). The available Ex R_x guidelines for cancer survivors (3, 4, 16, 17) broadly focus on the general well-being of

Authors' Affiliations: [1]University of Connecticut, Storrs, Connecticut; [2]Western New England College, Springfield, Massachusetts; and [3]National Cancer Institute, Bethesda, Maryland

Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

Corresponding Author: Justin C. Brown, Department of Kinesiology, University of Connecticut, 2095 N. Hillside Road, U-1110, Storrs, CT 06269. Phone: (860)-486-2812, Fax: (860)-486-3149. E-mail: justin.brown@uconn.edu

doi: 10.1158/1055-9965.EPI-10-0988

Published OnlineFirst November 4, 2010; DOI: 10.1158/1055-9965.EPI-10-0988

cancer survivors, encouraging 150 min/wk of aerobic exercise, 2 d/wk of strength training, and flexibility exercise on days when aerobic or resistance exercise is not performed. An American College of Sports Medicine (ACSM) panel of experts in Ex R_x for cancer survivors recently concluded exercise is safe for cancer survivors, all cancer survivors should avoid inactivity, and exercise programs should be adapted for the individual survivor on the basis of health status, cancer treatment type, targeted health outcomes, and disease trajectory (4). Yet, the panel acknowledged research in the area of Ex R_x for cancer survivors is in the developmental stage with significant research gaps in the dose of exercise required to ensure that cancer survivors receive safe and effective Ex R_x for targeted disease end points such as CRF.

We conducted a qualitative review evaluating the efficacy of exercise as an intervention to reduce CRF among adult cancer survivors. The primary purpose was to investigate which Ex R_x characteristics were associated with the greatest reductions in CRF. We also examined whether study methodologic considerations and subject characteristics combined or interacted with the dose of exercise prescribed to reduce CRF further.

Methods

Inclusion criteria

Included were randomized controlled trials (RCT) that examined the effects of exercise on CRF in adult patients (≥18 years) diagnosed with any type of cancer, stage of diagnosis, and type or stage of treatment including those who have completed treatment. Exercise interventions may have occurred in any setting with or without supervision. RCTs may have compared exercise with a usual care group receiving either (a) standard, usual care (e.g., no exercise program prescribed and to maintain current activity levels) or (b) non–exercise-related information during the intervention period. (See Supplementary Appendix I for detailed systematic search information)

CRF outcome measure

The outcome variable examined was patient-reported CRF (3), which studies assessed either separately or as a component of a comprehensive psychological questionnaire with a CRF subscale (see footnotes, Table 1; refs. 18–23).

Coding and reliability

Two independent raters (J.C.B, S.M.P) coded information related to the study (see Table 1). Intensity of exercise was estimated using metabolic equivalent units (MET), where 1 MET = 3.5 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$. Corresponding MET values for a given exercise intervention were coded from the Compendium of Physical Activity; these include low (<3 METs), moderate (3–≥6 METs), and vigorous (>6 METs) intensity levels (24). *Methodologic quality* was assessed via the Physiotherapy Evidence Database scale (PEDro). PEDro guidelines categorize high-quality studies from 6 to 11, fair quality from 4 to 5, and poor quality less than 4. Reliability of the raters was high across dimensions [*M* Cohen κ (ref. 25) = 0.78 for categorical variables, *M* Spearman-Brown reliability (ref. 26) = 0.90 for continuous variables]. Disagreements between coders were resolved through discussion.

Study outcomes and calculation of effect sizes

Because a majority of RCTs reported continuous measures, effect sizes (d) were defined as the standardized mean difference between the exercise and control groups divided by the pooled standard deviation, correcting for sample size bias and baseline differences (27). Multiple effect sizes were calculated from individual studies when they included more than 1 exercise intervention group (e.g., aerobic and resistance training groups compared with a control group). Subsequent sensitivity analyses were conducted to confirm the dependence did not influence mean estimates (28). Consequently, the 44 included studies provided 48 exercises versus control group comparisons.

Prior to analysis, data were assessed for publication bias using Begg (29; $z = 1.01$, $P = 0.31$) and Egger (30; $t = 0.06$, $P = 0.95$) methods, and yielded no evidence of publication bias (Fig. 3 funnel plot, Supplementary). The trim-and-fill technique (31) identified no added or omitted studies that were necessary to normalize the effect size distribution. Analyses were conducted in Stata 10.1 with macros for meta-analysis (32). The homogeneity statistic, Q, was calculated to determine whether a weighted mean effect size (d_+) characterized a common effect size. A significant Q indicated the absence of homogeneity (i.e., more variation in effect sizes than sampling error alone would predict). To standardize Q, the I^2 statistic and its 95% CI were calculated (33, 34). I^2 ranges from 0% to 100% with low values suggesting homogeneity and large values suggesting heterogeneity. To explain variability in the effect size estimates, the relation between study-level characteristics and the magnitude of the effects, was examined in modified least-squares regression analysis with the weights equivalent to the variance for each study effect size (viz., meta-regression). Bivariate analysis was conducted using fixed-effects assumptions, and the final, multimoderator analysis was conducted using random-effects assumptions. To reduce multicollinearity in multiple moderator models, all retained continuous moderators were zero centered and categorical variables were contrast coded.

Results

Potentially relevant reports included 7,245 articles of which 44 (n = 3,254) satisfied the selection criteria (Figure 1). Of the studies identified, 40 provided 1 CRF effect size estimate and 4 studies provided 2 estimates, yielding 48 effect sizes among 44 studies (see Table 1 for

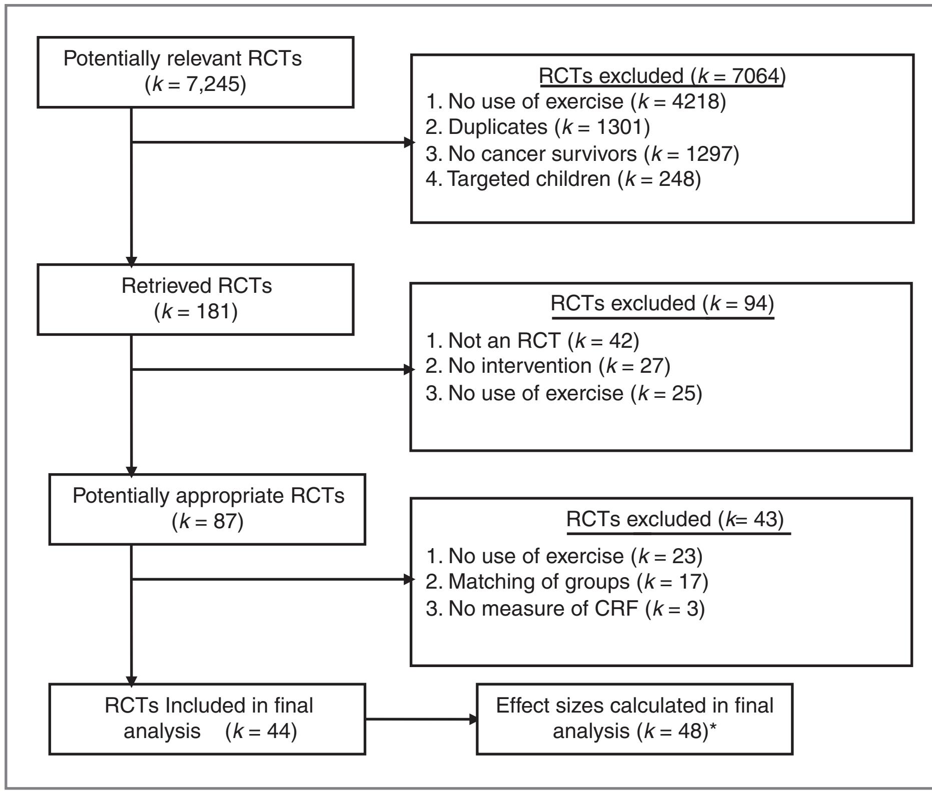

Figure 1. Flow diagram of trial identification and selection. *Four studies provided two interventions, yielding 2 effect size calculations.

descriptive statistics). Studies providing 2 effect sizes included 2 independent exercise intervention groups that were compared with 1 standard care group (46, 49, 55, 69). Three interventions with multiple intervention groups were randomized to aerobic exercise, resistance exercise, or control condition (49, 55, 69); whereas, the fourth study randomized participants to either supervised exercise, unsupervised exercise, or a control condition (46). The mean methodologic quality of the 44 included studies was 6.8 (1.4) of 11 (range: 3–10; Table 2).The mean age of cancer survivors was 53.8 (10.5) years and they averaged 6.7 (13.8) months postdiagnosis. The majority of cancer survivors were women (86%). Approximately, half (46%) of the cancer survivors were currently being treated with primary pharmacologic therapy during the exercise intervention. For those undergoing therapy, a majority of cancer survivors in the sample (75%) were being treated with a combination of chemotherapy and radiotherapy, whereas 13% were treated with only chemotherapy, 6% were treated with only radiation, and 6% were treated with only hormone therapy.

Twenty-five studies examined exercise interventions exclusively in breast cancer survivors (44–55, 57–68), 4 in prostate cancer survivors (69–72), 4 in lymphoma (73–76), 1 in leukemia (78), and 1 in colorectal cancer (77). The remaining 9 studies examined exercise interventions in a mixed group of cancer survivors (35–43). Twenty-four studies included only aerobic exercise (35, 38, 39, 42–44, 46, 49, 50, 52–59, 61, 65, 69, 70, 74, 77, 78), 6 studies included only resistance exercise (49, 55, 63, 68, 69, 71), 11 studies included a combination of aerobic and resistance exercise (40, 41, 48, 51, 60, 62, 64, 67, 72, 75, 76), and another 6 included neuromuscular exercise such as tai-chi or yoga (refs. 36, 37, 45, 47, 66, 73; Table 5 characteristics of included studies, Supplementary).

The average length of the exercise intervention was 11.5 (5.2) weeks. Cancer survivors exercised 3.5 (1.4) d/wk for 48.5 (22.8) minutes per session. The level of physical exertion or average intensity of the aerobic exercise interventions was 5.6 (3.0) METs, corresponding to moderate-intensity exercise (40%–60% V_{O_2}max), and included walking (48%), stationary cycle ergometry (30%), a combination of walking and cycling (16%), or other modalities of aerobic exercise such as the elliptical trainer or self-selected (6%). The average intensity of resistance training was 4.5 (2.0) METs, corresponding to moderate-intensity exercise (60%–80% 1-repetition maximum, 1-RM), and included weight machines, resistance bands, or free weights (75%). The remaining studies prescribed neuromuscular exercise which commonly included tai-chi or yoga (25%). Flexibility exercise was a component of the exercise in 52% of the exercise interventions. Supervision of exercise sessions was provided in 60% of the exercise interventions.

Ten studies used a theoretical basis for the exercise intervention (44, 48, 50, 54, 57–59, 61, 62, 65). Three

Published OnlineFirst November 4, 2010; DOI: 10.1158/1055-9965.EPI-10-0988

Table 1. Descriptive characteristics of included studies (means ± SD, except where noted)

Descriptive characteristic	All cancer	Breast	Prostate	Lymphoma
Study characteristics				
Number of studies, *k*	44	25	4	4
Year of study	2005 (3.5)	2004 (3.4)	2006 (2.7)	2006 (3.4)
Use of theory, %	27	22	0	0
Published in journal, %	88	84	100	100
Subject characteristics				
Age	53.8 (10.5)	52.6 (4.4)	67.9 (1.6)	49.8 (7.4)
Type of treatment, %				
Chemotherapy	13	12	0	25
Radiation	6	8	0	0
Hormones	6	4	80	0
Combination	75	76	20	75
Stage of treatment, %				
Currently treated	46	33	80	100
Previously treated	54	66	20	0
Time since diagnosis, mo	6.7 (13.8)	6.9 (13.1)	6.4 (14.3)	7.3 (14.6)
Intervention characteristics				
Intervention length, wk	11.5 (5.2)	11.8 (4.4)	16.0 (7.5)	12.3 (8.3)
Frequency, d/wk	3.5 (1.4)	3.4 (1.1)	2.6 (0.4)	3.3 (1.7)
Length, min/session	48.5 (22.8)	46.6 (21.9)	60.0 (18.4)	60.0 (21.2)
Aerobic intensity, METs	5.6 (3.0)	4.9 (2.1)	4.9 (5.2)	5.6 (3.5)
Strength intensity, METs	4.5 (2.0)	4.5 (1.7)	2.4 (3.2)	2.0 (1.2)
Flexibility, %				
Included	52	60	40	50
Excluded	48	40	60	50
CRF scale used, %				
FACT	30	36	60	25
Piper fatigue	20	32	0	0
POMS	13	8%	0%	25%
Brief fatigue index	11	4	0	0
Linear analog scale	4	4	0	0
EORTC QOL-C30	11	0	20	25
Other	11	16	20	25

Abbreviations: FACT, functional assessment of cancer therapy; POMS, profile of mood states; EORTC QOL-C30, European organization for research treatment center quality of life-care 30. Percentages may not sum to 100% due to rounding error.

interventions (48, 58, 62) followed the Transtheoretical model of behavior change (79, 80), 2 studies (54, 57) followed the model of self-efficacy and stages of exercise change (81), 3 studies (50, 59, 61) followed the Roy adaptation model (82), 1 study (44) followed the Payne adaptation model (83) and 1 study (65) followed the Levine conservation model (84).

Overall efficacy of exercise interventions on modulation of CRF

Table 3 summarizes weighted mean effect sizes, d_+, for all cancer types collectively, as well as cancer type individually. This analysis indicated that exercise reduced CRF (Table 3 and Fig. 2), yet its impact did not attain significance for survivors of lymphoma, colorectal, or leukemia cancer, which may have lacked sufficient statistical power to detect a difference. Pooled, the effect sizes for the 48 interventions lacked homogeneity, as did the collection of studies addressing breast cancer survivors.

Factors related to the magnitude of CRF modulation

Bivariate regression analyses examined potential sample, methodologic, and exercise intervention characteristics. Significant bivariate models were then integrated into a combined moderator model to explain unique study variance (Table 4). When integrated, the following moderators no longer remained significant: session length (minutes), number of exercise sessions, and treatment with radiation therapy. Four moderators impacting

Published OnlineFirst November 4, 2010; DOI: 10.1158/1055-9965.EPI-10-0988

Table 2. Methodologic quality of included studies by cancer type

Citation	Total	Study quality dimension 1	2	3	4	5	6	7	8	9	10	11
Thorsen (35)	7	+	+	−	+	−	−	−	+	+	+	+
Brown (36)	7	+	+	−	+	−	−	−	+	+	+	+
Culos-Reed (37)	7	+	+	−	+	−	−	−	+	+	+	+
Dimeo (38)	6	+	+	−	+	−	−	−	−	+	+	+
Dimeo (39)	7	+	+	−	+	−	−	−	+	+	+	+
Adamsen (40)	10	+	+	+	+	−	+	+	+	+	+	+
Mustain (41)	8	+	+	+	+	−	−	−	+	+	+	+
Burnham (42)	7	+	+	−	+	−	−	−	+	+	+	+
Shang (43)	7	+	+	−	+	−	−	−	+	+	+	+
Breast cancer												
Payne (44)	5	+	+	−	+	−	−	−	+	+	−	−
Galantino (45)	4	+	+	−	−	−	−	−	+	−	−	+
Segal (46)	7	+	+	−	+	−	−	−	+	+	+	+
Carson (47)	7	+	+	−	+	−	−	−	+	+	+	+
Mutrie (48)	10	+	+	+	+	−	+	+	+	+	+	+
Courneya (49)	7	+	+	−	+	−	−	−	+	+	+	+
Mock (50)	7	+	+	−	+	−	−	−	+	+	+	+
McKenzie (51)	8	+	+	−	+	−	−	−	+	+	+	+
Courneya (52)	9	+	+	−	+	−	+	+	+	+	+	+
Drouin (53)	6	+	+	−	+	−	−	−	+	−	+	+
Daley (54)	7	+	+	−	+	−	−	−	+	+	+	+
Yuen (55)	6	+	+	−	+	−	−	−	+	−	+	+
Courneya (56)	8	+	+	−	+	−	−	+	+	−	+	+
Pinto (57)	6	+	+	−	+	−	−	−	+	−	+	+
Pinto (58)	5	+	+	−	−	−	−	−	+	−	+	+
Mock (61)	5	+	+	−	+	−	−	−	+	−	+	−
Heim (60)	6	+	+	−	+	−	−	−	+	−	+	+
Mock (61)	4	+	+	−	+	−	−	−	−	−	+	−
Campbell (62)	6	+	+	−	−	−	−	−	+	+	+	+
Headley (63)	3	+	+	−	−	−	−	−	+	−	−	−
Milne (64)	8	+	+	+	+	−	−	−	+	+	+	+
Caldwell (65)	7	+	+	−	+	−	−	−	+	+	+	+
Vito (66)	7	+	+	−	+	−	−	−	+	+	+	+
Battaglini (67)	8	+	+	−	+	−	−	+	+	+	+	+
Barfoot (68)	7	+	+	−	+	−	−	−	+	+	+	+
Prostate cancer												
Segal (69)	6	+	+	−	+	−	−	−	−	+	+	+
Windsor (70)	6	+	+	−	+	−	−	−	+	−	+	+
Segal (71)	10	+	+	+	+	−	+	+	+	+	+	+
Galvao (72)	9	+	+	+	+	−	−	+	+	+	+	+
Lymphoma												
Cohen (73)	9	+	+	+	+	−	−	−	+	+	+	+
Courneya (74)	7	+	+	−	+	−	−	−	+	+	+	+
Jarden (75)	7	+	+	−	+	−	−	−	+	+	+	+
Coleman (76)	5	+	+	−	+	−	−	−	−	+	+	−
Colorectal												
Courneya (77)	7	+	+	−	+	−	−	+	+	+	+	+
Leukemia												
Chang (78)	6	+	+	−	+	−	−	−	+	−	+	+

NOTE: 1, eligibility criteria; 2, randomization; 3, concealed allocation; 4, baseline similarity of groups; 5, subject blinding; 6, therapist blinding; 7, assessor blinding; 8, outcome measure from >85% of subjects; 9, "intention to treat"; 10, between group statistical comparisons; and 11, point & variability measure.

Published OnlineFirst November 4, 2010; DOI: 10.1158/1055-9965.EPI-10-0988

Table 3. Weighted mean effect of exercise modulating CRF by type of cancer

		d_+ (95%CI)		Homogeneity of *ds*		
Type of cancer	k	Fixed-effects	Random-effects	*Q*	*P*	I^2 (95% CI)
All cancers	44[a]	0.312 (0.249–0.375)	0.310 (0.217–0.403)	93.37	<0.001	50% (30–64)
Breast	25[b]	0.388 (0.303–0.472)	0.391 (0.268–0.514)	47.16	<0.001	42% (10–63)
Prostate	4[c]	0.420 (0.270–0.570)	0.420 (0.270–0.570)	3.15	0.533	0% (0–96)
Lymphoma	4	0.199 (−0.025 to 0.425)	0.199 (−0.025 to 0.425)	2.32	0.508	0% (0–99)
Colorectal	1	0.057 (−0.469 to 0.583)	–	–	–	–
Leukemia	1	0.779 (−0.141 to 1.700)	–	–	–	–

NOTE: Weighted mean effect size values (d_+) are positive when the exercise intervention was successful in reducing CRF compared with standard care. *k*, number of studies.
[a]44 studies provided a total of 48 effect sizes.
[b]25 studies provided a total of 28 effect sizes.
[c]4 studies provided a total of 5 effect sizes.

CRF modulation in adult cancer survivors remained significant. Reductions in CRF were greater to the extent interventions: (i) adhered to a theoretical model (compared with those that did not do so; $\beta = 0.48$, $P = <0.001$); (ii) sampled older cancer survivors ($\beta = 0.24$, $P = 0.04$); and (iii), the greatest reductions in CRF occurred with moderate-intensity (3–6 METs, 60%–80%, 1-RM) resistance exercise ($\beta = 0.60$, $P = 0.01$), particularly for higher quality interventions (interaction $\beta = 0.23$, $P < 0.05$). In contrast, lower quality interventions were efficacious in reducing CRF at low (<3 METs) and moderate-intensity (3–6 METs, 60%–80% 1-RM) resistance exercise. Intensity of resistance exercise, use of theory, age, and methodologic quality together explained 52% of the variance among exercise interventions for adult cancer survivors. The estimates in Table 4 reveal that exercise interventions of moderate-intensity (3–6 METs, 60%–80% 1-RM) resistance exercise were successful in reducing CRF, regardless of the use of theory in the exercise intervention, age of the cancer survivor, and methodologic intervention quality. In contrast, interventions of low-intensity resistance (<3 METs, <60% 1-RM) exercise showed no significant reduction of CRF when theory was absent or in high methodologic quality interventions. Time since diagnosis, aerobic exercise, flexibility exercise, or supervision of exercise sessions did not moderate CRF modulation.

Discussion

Overall, we found that exercise moderately reduced CRF among cancer survivors with an effect size of 0.31 (95% CI: 0.22–0.40), consistent with prior reviews (12, 15). Of note is our new finding that resistance exercise has a positive, quadratic, and exercise intensity dose response effect on CRF. For cancer survivors engaging in moderate-intensity, resistance exercise (3–6 METs, 60%–80% 1-RM) reduced CRF more so than those engaging in lower intensity resistance or aerobic exercise of any level of physical exertion. Another interesting finding was that exercise interventions based on a theoretical model of behavior change or adaptation were more successful in reducing CRF than those interventions not based on such models. Age was also related to CRF reduction, with older cancer survivors reducing CRF to greater levels than younger cancer survivors. Lastly, RCTs of stronger methodologic quality (i.e., higher PEDro score) reduced CRF less than those of weaker methodologic quality. Our findings about exercise interventions based on theoretical models and of higher methodologic quality support previous meta-analytic work examining the influence of exercise on CRF (11). They also update the literature with a larger, more diverse sample of cancer survivors, and types of exercise interventions (11).

Subgroup analysis relating to cancer type revealed that exercise moderately reduced CRF, 0.39 (95% CI: 0.27–0.51) and 0.42 (95% CI: 0.27–0.57), among breast and prostate cancer survivors, respectively. These findings update and support previous meta-analytic reviews advocating the use of exercise as a nonpharmacologic intervention to reduce CRF among breast and prostate cancer survivors (11, 12). Subgroup analysis among leukemia, lymphoma, and colorectal cancer survivors yielded nonsignificant reductions in CRF.

Four meta-analyses have been conducted examining the effect of exercise on CRF (11–14). Two of these meta-analysis have examined the mean reduction of exercise on CRF (13, 14) without accounting for exercise characteristics that may moderate the efficacy of exercise on CRF. The remaining 2 meta-analyses (11, 12) have examined moderators relating to the efficacy of exercise in reducing CRF; however, these meta-analyses were composed of a smaller number of studies [i.e., 17 (11) and 18 studies (12)] and did not examine specific Ex R_x characteristics included in our analysis that may impact CRF modulation. In our meta-analysis of 48 interventions, we found that exercise intensity was a significant moderator

Published OnlineFirst November 4, 2010; DOI: 10.1158/1055-9965.EPI-10-0988

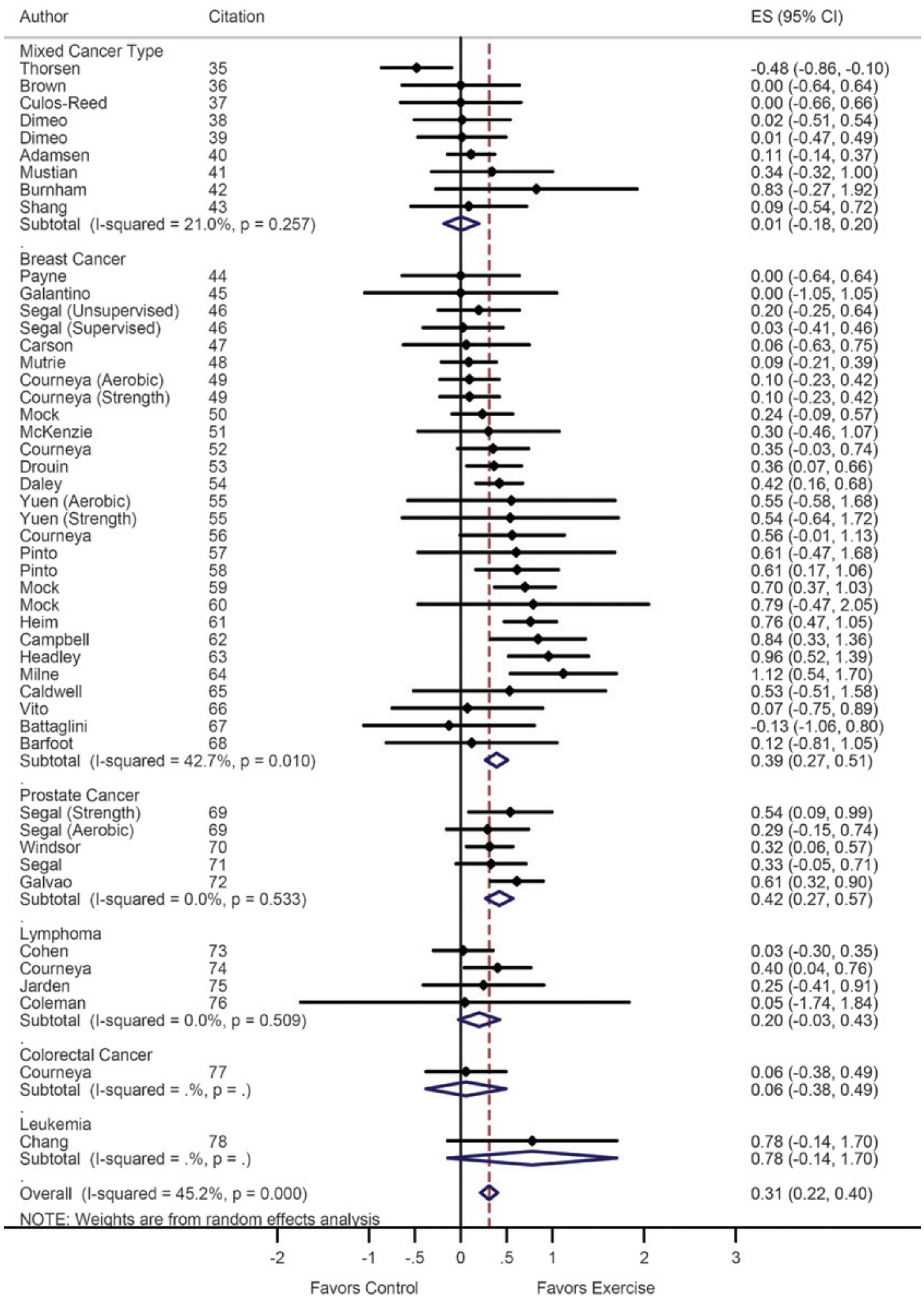

Figure 2. Forest plot of effect sizes gauging impact of exercise on CRF modulation by cancer type with random-effects means.

Published OnlineFirst November 4, 2010; DOI: 10.1158/1055-9965.EPI-10-0988

Table 4. Intervention characteristics related to CRF reduction for all cancer survivors, showing estimates at light and moderate levels of resistance exercise

		Estimates of d_+ (95% CI)[b] Intensity of resistance exercise	
Study dimension	**Level[a]**	**Light (2.0 METs)**	**Moderate (6.0 METs)**
Use of theory	Absent	−0.034 (−0.207 to 0.139)	0.361 (0.141–0.582)
	Present	0.354 (0.177–0.531)	0.749 (0.470–1.029)
Age, y	39	0.160 (0.009–0.311)	0.555 (0.319–0.791)
	65	0.385 (0.205–0.564)	0.780 (0.589–0.971)
	70	0.428 (0.214–0.643)	0.823 (0.612–1.035)
Intervention quality	Highest (PEDro = 10)	0.010 (−0.197 to 0.217)	0.594 (0.310–0.879)
	Mean (PEDro = 6.8)	0.289 (0.165–0.413)	0.684 (0.506–0.862)
	Lowest (PEDro = 3)	0.631 (0.363–0.900)	0.794 (0.339–1.249)

NOTE: Weighted mean effect size values (d_+) are positive when the exercise intervention was successful in reducing CRF compared to standard care. MET values were provided to demonstrate the emerging patterns among theory, age, and intervention quality with increasing resistance exercise intensity, representing light (2.0 MET) and moderate (6.0 MET) intensity.

[a]Levels represent values at the extreme observations of each moderator and for other values of interest within that range.

[b]d_+ and their 95% CI estimates statistically adjust for the presence of the moderators in the mixed-effects model, including the linear and quadratic trends for strength intensity, use of theory, age, and intervention quality, held constant at their means except for differences in strength intensity and the study dimension in question.

of CRF among adult cancer survivors participating in resistance training programs. A positive, quadratic pattern emerged suggesting that moderate-intensity resistance exercise interventions were more efficacious in diminishing CRF than those of lower intensity or aerobic exercise of any level of intensity. Our finding of the efficacy of resistance exercise reducing CRF was somewhat unexpected. Current exercise guidelines for cancer survivors emphasize the importance of participating in aerobic exercise, complimented with resistance and flexibility exercises (ACSM Roundtable; ref. 4) and often make no (National Comprehensive Cancer Network; ref. 3) or minimal mention (American Cancer Society; ref. 17) of resistance exercise.

A possible mechanism for the effectiveness of resistance exercise in reducing CRF among breast and prostate cancer survivors is the attenuation of the progressive muscle wasting and disruptions in muscle metabolism that occur with cancer and associated treatments (85). Several hypotheses related to muscle protein synthesis, ATP dysregulation, cytokine dysregulation, and progressive muscle wasting have all been postulated as mechanistic underpinnings of CRF (85, 86). Moderate-intensity resistance training increases muscle protein synthesis (87), improves cytokine response (88), and diminishes the rate of sarcopenia (89) among healthy human populations as well as those with compromised muscle function such as those with cerebral palsy and other musculoskeletal disorders (90). Further, recent evidence suggests that resistance exercise may provide health benefits such as improved total body muscular strength, self-esteem, and vitality in breast and prostate cancer survivors (49, 72, 91).

Another interesting finding was that older cancer survivors reduced CRF to greater levels than younger cancer survivors engaging in any form of exercise. This finding is of particular importance as most cancer survivors are older ≥65 years (1), yet most exercise interventions have focused on younger cancer survivors (4). Older cancer survivors are frequently challenged with age-related declines in health (i.e., sarcopenia, decreased functional capacity) as well as cancer-related declines in health (e.g., cachexia, body composition changes, decreased bone mineral density; ref. 92). Exercise has been shown to elicit favorable health outcomes among older prostate cancer survivors including, increased lean body mass and muscle strength, and increase distance walked in 6 minutes (72). Improving the status of these health parameters (e.g., body composition, muscular strength, and cardiorespiratory fitness) may influence the mediation of CRF among other populations of cancer survivors.

Exercise interventions that adhered to a theoretical model of behavior change (86, 88) or adaptation model (82) achieved larger reductions in CRF than those that did not adhere to such models. Theoretical models provide empirically supported frameworks that inform behavior change and may offer useful information about determinants of exercise behavior (93, 94). An understanding of exercise behavior and behavioral determinants among cancer survivors may help clinicians identify specific intervention strategies to facilitation adoption and maintenance of an existing exercise program in this population. Theoretical models of adaptation for cancer survivors may be efficacious in improving psychological components of mental health (e.g., distress of cancer diagnosis) potentially influencing CRF modulation. Despite the promise of such interventions, relatively few of the studies implementing a theoretical framework elaborated on the specific role of theory in the exercise intervention. Therefore, the current meta-analysis is limited in its ability to determine the specific underpinnings of theory mediating the reduction in CRF.

This study is subject to several limitations. Despite our comprehensive review of the literature examining CRF in all types of cancer, our search yielded 28 of the 48 exercise interventions that targeted breast (58%) and prostate cancer (10%) survivors exclusively. The large number of interventions examining the impact of exercise on CRF modulation among breast cancer survivors limits the generalizability of our findings to other types of cancer survivors. Moreover, we acknowledge that theories of behavior change and adaptation models are hypothesized to influence fatigue through different mechanisms. As noted, we combined them into a single category because there were relatively few instantiations of theory-led interventions. Despite this limitation, the efficacy of the application of either behavior changes or adaptation models is promising when compared with those not adhering to a prespecified theory or model.

Another limitation relates to the major finding of this meta-analysis, that moderate-intensity resistance exercise may be beneficial in reducing CRF. In particular, no study examined resistance exercise interventions greater than 6 METs (>80% 1-RM). It remains unknown if more vigorous-intensity resistance training would provide greater or lesser reductions in CRF. We did not evaluate adherence to the exercise interventions in this meta-analysis because most studies did not report this information. This variable should have important moderating effects on CRF modulation.

In summary, we confirm with the largest meta-analysis of RCTs conducted to date that moderate resistance exercise reduces CRF among adult cancer survivors, particularly breast and prostate cancer survivors and those of older age. Cancer survivors engaging in moderate-intensity resistance exercise modulated CRF levels more than those engaging in low-intensity resistance exercise or low to moderate intensity, aerobic exercise. Further, the most efficacious exercise interventions were based on behavior change and adaptation theory. Our findings reinforce the notion that exercise interventions for adult cancer survivors should be individualized based on the targeted health outcome and possibly cancer type. In addition, exercise interventions should be multidimensional, combining sound exercise as well as behavioral science.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Acknowledgment

We thank Robert D. Siegel, M.D., Gray Cancer Center, Hartford Hospital for reviewing this manuscript and providing valuable feedback.

Grant Support

This research was supported by University of Connecticut Research Foundation Grant 433527 (PIs: B.T. Johnson and L.S. Pescatello)

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received September 15, 2010; revised October 23, 2010; accepted October 25, 2010; published OnlineFirst November 3, 2010.

References

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA Cancer J Clin 2009;59:225–49.
2. Crom DB, Hinds PS, Gattuso JS, Tyc V, Hudson MM. Creating the basis for a breast health program for female survivors of hodgkin disease using a participatory research approach. Oncol Nurs Forum 2005;32:1131–41.
3. NCCN clinical practice guidelines in oncology. Cancer-related fatigue. J Natl Compr Cancer Netw 2010;8:904–931.
4. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefriend W, Galvao, DA, Pinto, BM, et al. American college of sports medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc 2010;42:1409–26.
5. Hofman M, Ryan JL, Figueroa-Moseley CD, Jean-Pierre P, Morrow GR. Cancer-related fatigue: the scale of the problem. Oncologist 2007; 12Suppl 1:4–10.
6. Servaes P, Verhagen S, Bleijenberg G. Determinants of chronic fatigue in disease-free breast cancer patients: a cross-sectional study. Ann Oncol 2002;13:589–98.
7. Dow KH, Ferrell BR, Leigh S, Ly J, Gulasekaram P. An evaluation of the quality of life among long-term survivors of breast cancer. Breast Cancer Res Treat 1996;39:261–73.
8. Janda M, Gerstner N, Obermair A, Obermair A, Fuerst A, Wachter S, et al. Quality of life changes during conformal radiation therapy for prostate carcinoma. Cancer 2000;89: 1322–8.
9. Ferrer RA, Huedo-Medina TB, Johnson BT, Ryan S, Pescatello LS. Exercise interventions for cancer-surviviors: a meta-analysis of quality of life outcomes. Ann Behav Med 2010. Epub 2010 Oct 8.
10. Courneya KS, Friedenreich CM, Sela RA, Quinney HA, Rhodes RE, Handman M. The group psychotherapy and home-based physical exercise (group-hope) trial in cancer survivors: physical fitness and quality of life outcomes. Psychooncology 2003; 12:357–74.
11. Kangas M, Bovbjerg DH, Montgomery GH. Cancer-related fatigue: a systematic and meta-analytic review of non-pharmacological therapies for cancer patients. Psychol Bull 2008;134:700–41.
12. Velthuis MJ, Agasi-Idenburg SC, Aufdemkampe G, Wittink HM. The effect of physical exercise on cancer-related fatigue during cancer treatment: a meta-analysis of randomised controlled trials. Clin Oncol (R Coll Radiol). 2010;22:208–21.
13. Schmitz KH, Holtzman J, Courneya KS, Masse LC, Duval S, Kane R. Controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. Cancer Epidemiol Biomarkers Prev 2005;14:1588–95.
14. Speck RM, Courneya KS, Masse LC, Duval S, Schmitz KH. An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. J Cancer Surviv 2010;4:87–100.
15. Cramp F, Daniel J. Exercise for the management of cancer-related fatigue in adults. Cochrane Database Syst Rev 2008;2:CD006145.

16. Thompson WR, Gordon NF, Pescatello LS, editors. ACSM's Guidelines for Exercise Testing and Prescription. 8th ed. Lippincott WIlliams & Wilkins; 2010.
17. Doyle C, Kushi LH, Byers T, Courneya KS, Demark-Wahnefried W, Grant B, et al. Nutrition and physical activity during and after cancer treatment: an american cancer society guide for informed choices. CA Cancer J Clin 2006;56:323–53.
18. Yellen SB, Cella DF, Webster K, Blendowski C, Kaplan E. Measuring fatigue and other anemia-related symptoms with the functional assessment of cancer therapy (FACT) measurement system. J Pain Symptom Manage 1997;13:63–74.
19. Piper BF, Dibble SL, Dodd MJ, Weiss MC, Slaughter RE, Paul SM. The revised piper fatigue scale: psychometric evaluation in women with breast cancer. Oncol Nurs Forum 1998;25:677–84.
20. Baker F, Denniston M, Zabora J, Polland A, Dudley WN. A POMS short form for cancer patients: psychometric and structural evaluation. Psychooncology 2002;11:273–81.
21. Mendoza TR, Wang XS, Cleeland CS, Morrissey M, Johnson BA, Wendt JK, et al. The rapid assessment of fatigue severity in cancer patients: use of the brief fatigue inventory. Cancer 1999;85:1186–96.
22. Locke DEC, Decker PA, Sloan JA, et al. Validation of single-item linear analog scale assessment of quality of life in neuro-oncology patients. J Pain Symptom Manage 2007;34:628–38.
23. Efficace F, Innominato PF, Bjarnason G, et al. Validation of patient's self-reported social functioning as an independent prognostic factor for survival in metastatic colorectal cancer patients: results of an international study by the chronotherapy group of the european organisation for research and treatment of cancer. J Clin Oncol 2008;26:2020–6.
24. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, et al. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc 2000;32Suppl:S498–504.
25. Cohen J. Weighted kappa: nominal scale agreement provision for scaled disagreement or partial credit. Psychol Bull 1968;70:213–20.
26. Bartko JJ. On various intraclass correlation reliability coefficients. Psychol Bull 1976;83:762–5.
27. Hedges LV, Olkin I. Statistical Methods for Meta-Analysis. Orlando, FL: Academic Press Inc; 1985.
28. Becker B.J.. Handbook of Applied Multivariate Statistics and Mathematical Modeling. In:Tinsley HEA , Brown SD , editors. San Diego, CA.: Academic Press; 2000. p. 499–525.
29. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994;50:1088–101.
30. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. Br Med J 1997;315:629–34.
31. Duval S, Tweedie R. A nonparametric ``trim and fill'' method of accounting for publication bias in meta-analysis. J Am Stat Assoc 2000;95:89–98.
32. Lipsey MW, Wilson DB. Practical Meta-AnalysisThousand Oaks, CA: Sage; 2001.
33. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539–58.
34. Huedo-Medina TB, Sanchez-Meca J, Marin-Martinez F, Botella J. Assessing heterogeneity in meta-analysis: q statistic or I2 index? Psychol Methods 2006;11:193–206.
35. Thorsen L, Skovlund E, Stromme SB, Hornslien K, Dahl AA, Fossa SD. Effectiveness of physical activity on cardiorespiratory fitness and health-related quality of life in young and middle-aged cancer patients shortly after chemotherapy. J Clin Oncol 2005;23:2378–88.
36. Brown P, Clark MM, Atherton P, Huschka M, Sloan JA, Gamble G, et al. Will improvement in quality of life (QOL) impact fatigue in patients receiving radiation therapy for advanced cancer?Am J Clin Oncol 2006;29:52–8.
37. Culos-Reed SN, Carlson LE, Daroux LM, Hately-Aldous S. A pilot study of yoga for breast cancer survivors: physical and psychological benefits. Psychooncology 2006;15:891–7.
38. Dimeo FC, Stieglitz RD, Novelli-Fischer U, Fetscher S, Keul J. Effects of physical activity on the fatigue and psychologic status of cancer patients during chemotherapy. Cancer 1999;85:2273–7.
39. Dimeo FC, Thomas F, Raabe-Menssen C, Propper F, Mathias M. Effect of aerobic exercise and relaxation training on fatigue and physical performance of cancer patients after surgery. A randomised controlled trial. Support Care Cancer 2004;12:774–9.
40. Adamsen L, Quist M, Andersen C. Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: randomised controlled trial. 2009;339:b3410.
41. Mustian KM, Peppone L, Darling TV, Palesh O, Heckler CE, Morrow GR. A 4-week home-based aerobic and resistance exercise program during radiation therapy: a pilot randomized clinical trial. J Support Oncol 2009;7:158–67.
42. Burnham TR, Wilcox A. Effects of exercise on physiological and psychological variables in cancer survivors. Med Sci Sports Exerc 2002;34:1863–7.
43. Shang J. Exercise adherence and contamination in a randomized control trial of a home-based walking program among patients receiving active cancer treatment [dissertation]. Baltimore (MD): Johns Hopkins University; 2009.
44. Payne JK, Held J, Thorpe J, Shaw H. Effect of exercise on biomarkers, fatigue, sleep disturbances, and depressive symptoms in older women with breast cancer receiving hormonal therapy. Oncol Nurs Forum 2008;35:635–42.
45. Galantino ML, Capito L, Kane RJ, Ottey N, Switzer S, Packel L. The effects of tai chi and walking on fatigue and body mass index in women living with breast cancer: a pilot study. Rehab Oncol 2003;21:17–22.
46. Segal R, Evans W, Johnson D, Smith J, Colletta S, Gayton J, et al. Structured exercise improves physical functioning in women with stages I and II breast cancer: results of a randomized controlled trial. J Clin Oncol 2001;19:657–65.
47. Carson JW, Carson KM, Porter LS, Keefe FJ, Seewaldt VL. Yoga of awareness program for menopausal symptoms in breast cancer survivors: results from a randomized trial. Support Care Cancer 2009;17:1301–9.
48. Mutrie N, Campbell AM, Whyte F, McConnachie A, Emslie C, Lee L, et al. Benefits of supervised group exercise programme for women being treated for early stage breast cancer: pragmatic randomised controlled trial. BMJ 2007;334:517.
49. Courneya KS, Segal RJ, Mackey JR, Gelmon K, Reid RD, Friedenreich CM, et al. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. J Clin Oncol 2007;25:4396–404.
50. Mock V, Frangakis C, Davidson NE, Ropka ME, Pickett M, Poniatowski B, et al. Exercise manages fatigue during breast cancer treatment: a randomized controlled trial. Psychooncology 2005;14:464–77.
51. McKenzie DC, Kalda AL. Effect of upper extremity exercise on secondary lymphedema in breast cancer patients: a pilot study. J Clin Oncol 2003;21:463–6.
52. Courneya KS, Friedenreich CM, Sela RA, Quinney HA, Rhodes RE, Handman M. The group psychotherapy and home-based physical exercise (group-hope) trial in cancer survivors: physical fitness and quality of life outcomes. Psychooncology 2003;12:357–74.
53. Drouin JS, Armstrong H, Krause S., Orr J, Birk TJ, Hryniuk WM. Effects of aerobic exercise training on peak aerobic capacity, fatigue, and psyhchological factors during radiation for breast cancer. Rehab Oncol 2005;1:11–7.
54. Daley AJ, Crank H, Saxton JM, Mutrie N, Coleman R, Roalfe A. Randomized trial of exercise therapy in women treated for breast cancer. J Clin Oncol 2007;25:1713–21.
55. Yuen HK, Sword D. Home-based exercise to alleviate fatigue and improve functional capacity among breast cancer survivors. J Allied Health 2007;36:e257–75.
56. Courneya KS, Mackey JR, Bell GJ, Jones LW, Field CJ, Fairey AS. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: cardiopulmonary and quality of life outcomes. J Clin Oncol 2003;21:1660–8.
57. Pinto BM, Clark MM, Maruyama NC, Feder SI. Psychological and fitness changes associated with exercise participation among women with breast cancer. Psychooncology 2003;12:118–26.
58. Pinto BM, Frierson GM, Rabin C, Trunzo JJ, Marcus BH. Home-based physical activity intervention for breast cancer patients. J Clin Oncol 2005;23:3577–87.

59. Mock V, Dow KH, Meares CJ, Grimm PM, Dienemann JA, Haisfield-Wolfe ME, et al. Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. Oncol Nurs Forum 1997;24:991–1000.
60. Heim ME, v d Malsburg ML, Niklas A. Randomized controlled trial of a structured training program in breast cancer patients with tumor-related chronic fatigue. Onkologie 2007;30:429–34.
61. Mock V, Burke MB, Sheehan P, Creaton EM, Winningham ML, McKenney-Tedder S, et al. A nursing rehabilitation program for women with breast cancer receiving adjuvant chemotherapy. Oncol Nurs Forum 1994;21:899,907; discussion 908.
62. Campbell A, Mutrie N, White F, McGuire F, Kearney N. A pilot study of a supervised group exercise programme as a rehabilitation treatment for women with breast cancer receiving adjuvant treatment. Eur J Oncol Nurs 2005;9:56–63.
63. Headley JA, Ownby KK, John LD. The effect of seated exercise on fatigue and quality of life in women with advanced breast cancer. Oncol Nurs Forum 2004;31:977–83.
64. Milne HM, Wallman KE, Gordon S, Courneya KS. Impact of a combined resistance and aerobic exercise program on motivational variables in breast cancer survivors: a randomized controlled trial. Ann Behav Med 2008;36:158–66.
65. Caldwell MG. The effects of an endurance exercise regime on cancer-related fatigue and physical performance in women with breast cancer. 2009.
66. Vito NL. The effects of a yoga intervention on physical and psychological functioning for breast cancer survivors. 2007.
67. Battaglini CLLG. A randomized study on the effects of a prescribed exercise intervention on lean mass and fatigue changes in breast cancer patients during treatment. 2004.
68. Barfoot DA. The effects of a resistance training protocol on changes in muscular strength and fatigue levels in breast cancer patients undergoing treatment. 2005.
69. Segal RJ, Reid RD, Courneya KS, et al. Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer. J Clin Oncol 2009;27:344–51.
70. Windsor PM, Nicol KF, Potter J. A randomized, controlled trial of aerobic exercise for treatment-related fatigue in men receiving radical external beam radiotherapy for localized prostate carcinoma. Cancer 2004;101:550–7.
71. Segal RJ, Reid RD, Courneya KS, et al. Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. J Clin Oncol 2003;21:1653–9.
72. Galvao DA, Taaffe DR, Spry N, Joseph D, Newton RU. Combined resistance and aerobic exercise program reverses muscle loss in men undergoing androgen suppression therapy for prostate cancer without bone metastases: a randomized controlled trial. J Clin Oncol 2010;28:340–7.
73. Cohen L, Warneke C, Fouladi RT, Rodriguez MA, Chaoul-Reich A. Psychological adjustment and sleep quality in a randomized trial of the effects of a tibetan yoga intervention in patients with lymphoma. Cancer 2004;100:2253–60.
74. Courneya KS, Sellar CM, Stevinson C, McNeely ML, Peddle CJ, Friedenreich CM, et al. Randomized controlled trial of the effects of aerobic exercise on physical functioning and quality of life in lymphoma patients. J Clin Oncol 2009;27:4605–12.
75. Jarden M, Baadsgaard MT, Hovgaard DJ, Boesen E, Adamsen L. A randomized trial on the effect of a multimodal intervention on physical capacity, functional performance and quality of life in adult patients undergoing allogeneic SCT. Bone Marrow Transplant 2009;43:725–37.
76. Coleman EA, Coon S, Hall-Barrow J, Richards K, Gaylor D, Stewart B. Feasibility of exercise during treatment for multiple myeloma. Cancer Nurs 2003;26:410–9.
77. Courneya KS, Friedenreich CM, Quinney HA, Fields AL, Jones LW, Fairey AS. A randomized trial of exercise and quality of life in colorectal cancer survivors. Eur J Cancer Care 2003;12:347–57.
78. Chang PH, Lai YH, Shun SC, Lin LY, Chen ML, Yang Y, et al. Effects of a walking intervention on fatigue-related experiences of hospitalized acute myelogenous leukemia patients undergoing chemotherapy: a randomized controlled trial. J Pain Symptom Manage 2008;35:524–34.
79. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. Am J Health Promot 1997;12:38–48.
80. Jones LW, Courneya KS, Vallance JK, Labha AB, Mant MJ, Belch AR, et al. Understanding the determinants of exercise intentions in multiple myeloma cancer survivors: an application of the theory of planned behavior. Cancer Nurs 2006;29:167–75.
81. Marcus BH, Selby VC, Niaura RS, Rossi JS. Self-efficacy and the stages of exercise behavior change. Res Q Exerc Sport 1992;63:60–6.
82. Roy C., Andrews H.A. The Roy Adaptation Model. The Definitive Statement. Norwalk, CT: Appleton & Lange; 1991.
83. Payne JK. A neuroendocrine-based regulatory fatigue model. Biol Res Nurs 2004;6:141–50.
84. Schaefer KM, Pond JB. Levine's conservation model as a guide to nursing practice. Nurs Sci Q 1994;7:53–4.
85. Ryan JL, Carroll JK, Ryan EP, Mustian KM, Fiscella K, Morrow GR. Mechanisms of cancer-related fatigue. Oncologist 2007;12 Suppl 1:22–34.
86. Al-Majid S, Gray DP. A biobehavioral model for the study of exercise interventions in cancer-related fatigue. Biol Res Nurs 2009;10:381–91.
87. Phillips SM, Tipton KD, Aarsland A, Wolf SE, Wolfe RR. Mixed muscle protein synthesis and breakdown after resistance exercise in humans. Am J Physiol. 1997;273:E99–107.
88. Petersen AMW, Pedersen BK. The anti-inflammatory effect of exercise. J Appl Physiol 2005;98:1154–62.
89. Doherty TJ. Invited review: aging and sarcopenia. J Appl Physiol. 2003;95:1717–27.
90. Taylor NF, Dodd KJ, Damiano DL. Progressive resistance exercise in physical therapy: a summary of systematic reviews. Phys Ther 2005;85:1208–23.
91. Galvao DA, Nosaka K, Taaffe DR, Peake J, Spry N, Suzuki K, et al. Endocrine and immune responses to resistance training in prostate cancer patients. Prostate Cancer Prostatic Dis 2008;11:160–5.
92. Courneya KS, Vallance JK, McNeely ML, Karvinen KH, Peddle CJ, Mackey JR. Exercise issues in older cancer survivors. Crit Rev Oncol Hematol 2004;51:249–61.
93. Fishbein M. The role of theory in HIV prevention. AIDS Care2000;12: 273–8.
94. Prochaska JO, Velicer WF, Rossi JS, Goldstein MG, Marcs BH, Rakowski W, et al. Stages of change and decisional balance for 12 problem behaviors. Health Psychol 1994; 13:39–46.
95. Jacobsen PB, Donovan KA, Vadaparampil ST, Small BJ. Systematic review and meta-analysis of psychological and activity-based interventions for cancer-related fatigue. Health Psychol 2007; 26:660–7.
96. Kuchinski AM, Reading M, Lash AA. Treatment-related fatigue and exercise in patients with cancer: a systematic review. Medsurg Nurs 2009;18:174–80.
97. Lotfi-Jam K, Carey M, Jefford M, Schofield P, Charleson C, Aranda S. Nonpharmacologic strategies for managing common chemotherapy adverse effects: a systematic review. J Clin Oncol 2008;26:5618–29.
98. Luctkar-Flude MF, Groll DL, Tranmer JE, Woodend K. Fatigue and physical activity in older adults with cancer: a systematic review of the literature. Cancer Nurs 2007;30:E35–45.
99. Stevinson C, Lawlor DA, Fox KR. Exercise interventions for cancer patients: systematic review of controlled trials. Cancer Causes Control 2004;15:1035–56.

Cancer Epidemiology, Biomarkers & Prevention

American Association for Cancer Research

Efficacy of Exercise Interventions in Modulating Cancer-Related Fatigue among Adult Cancer Survivors: A Meta-Analysis

Justin C. Brown, Tania B. Huedo-Medina, Linda S. Pescatello, et al.

Cancer Epidemiol Biomarkers Prev 2011;20:123-133. Published OnlineFirst November 4, 2010.