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ORIGINAL REPORT

Randomized Trial of Exercise Therapy in Women Treated for Breast Cancer

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ABSTRACT

Purpose
To examine the effects of aerobic exercise therapy on quality of life (QoL) and associated outcomes in women treated for breast cancer. Evidence suggests that exercise may be beneficial, but no trial has included an exercise-placebo and a usual-care group to control for the attention effects that might be associated with aerobic exercise interventions in cancer patients.

Patients and Methods
A total of 108 women who had been treated for breast cancer 12 to 36 months previously were randomly assigned to supervised aerobic exercise therapy (n = 34), exercise-placebo (body conditioning; n = 36), or usual care (n = 38). Exercise therapy and exercise-placebo sessions took place three times per week for 8 weeks. Outcomes included QoL, depression, exercise behavior, aerobic fitness; outcomes were assessed at baseline and at the 8- and 24-week follow-up.

Results
Analyses of covariance revealed a significant mean difference of 9.8 units in Functional Assessment of Cancer Therapy–General (primary outcome) favoring aerobic exercise therapy at 8 weeks, relative to usual care. Significant differences that favored aerobic exercise therapy relative to usual care were recorded for Functional Assessment of Cancer Therapy–Breast, social/family well-being, functional well-being, and breast cancer subscale scores at 8-week follow-up. Psychological health outcomes improved modestly for both intervention groups; these improvements were sustained for several end points.

Conclusion
Exercise therapy had large, clinically meaningful, short-term beneficial effects on QoL in women treated for breast cancer; this finding cannot be attributable to attention, given that the exercise-placebo group did not report similar effects relative to usual care.

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INTRODUCTION

Survival rates for breast cancer have been improving for more than 20 years and this appears likely to continue.[1] The estimated relative 5-year survival rate for women diagnosed in England and Wales in 2001 to 2003 was 80%.[1] However, breast cancer and its treatment sequelae are associated with significant changes in quality of life (QoL) and well-being[2] that may persist for many years.[3,4] Exercise interventions may be particularly appropriate in cancer populations because they have the potential to improve physical and psychological health simultaneously. Systematic review evidence[5-8] seems to favor QoL benefit from exercise, but reviews have raised concerns about the methodologic quality of previous studies. Improvements in QoL could be attributable to the increased attention given to cancer patients involved in exercise interventions, and a recent systematic review[6] highlighted the need for trials to include appropriate comparison groups to rule out the possibility of such effects. This is likely to be more of a concern in studies that involved a no-treatment usual-care arm. To date only four studies[9-12] have been designed to have at least partial ability to answer this question in cancer patients, but none included both exercise-placebo and usual-care comparison groups. Such comparisons provide the most rigorous examination of the efficacy of aerobic exercise as a QoL-enhancing intervention. This trial[13] was designed to address some of methodologic shortfalls of previous research.

PATIENTS AND METHODS

Participants, Recruitment Strategies, and Eligibility

The trial methodology has been reported previously.[13] The primary recruitment strategy was by postal invitation letter from patients' treating oncologist or surgeon, who identified potentially eligible patients from hospital records. Secondary recruitment strategies involved media advertisements and presentations to cancer support groups and breast cancer nurses. Women who were not regularly active and who had been treated for localized breast cancer 12 to 36 months previously were eligible. Women with metastases and inoperable or active locoregional disease were ineligible (clinician determined). The local research ethics committee provided ethical approval.

Additional Eligibility Screening

Interested patients contacted the study team by telephoning a dedicated number. Patients who were eligible according to age (18 to 65 years), diagnosis, and treatment criteria were screened for their current exercise behavior. Patients still considered eligible were invited subsequently to attend a familiarization session at the trial center, where they were screened further for contraindications to exercise using the Physical Activity Readiness Questionnaire.[14] Eligible patients were then asked to provide written informed consent.

Random Assignment to Treatment and Assessments

A telephone randomization service was provided by an independent trials unit. Randomization to the three treatment arms was on a 1:1:1 ratio and was performed using stratified random permuted blocks (with block size of six). Stratification factors were chemotherapy (yes/no) and tamoxifen (yes/no). Random assignment took place after the baseline assessments. Outcome assessors were not blinded to participants' group allocation. Assessments of outcomes took place at a university center and were completed at baseline, and 8 (primary end point) and 24 weeks follow-up. (An assessment of outcomes took place at 4 weeks from baseline for monitoring purposes and was not included in analyses). The trial researcher enrolled participants. Participants were informed they had a two out of three chance of being randomly assigned to one of the exercise intervention groups. Every effort was made to avoid communicating to patients the idea of stretching/body conditioning as a placebo or control. The same researcher delivered all sessions for both interventions.

Trial Interventions

Exercise therapy. Sessions took place at a university center, were one-to-one sessions with an exercise specialist, and lasted 50 minutes. In line with exercise guidelines for cancer patients,[15] participants exercised three times per week for 8 weeks. Heart rate (HR) and ratings of perceived exertion (RPE)[16] were assessed every 2 minutes during sessions. Exercise therapy sessions involved moderate-intensity exercise[13] (65% to 85% of age-adjusted HR maximum and RPE of 12 to 13). A variety of cognitive-behavioral techniques[17] for promoting exercise behavior change were explored with participants during sessions.[13]

Exercise-Placebo and Usual Care

The exercise-placebo group also attended 24 one-to-one 50-minute sessions during 8 weeks; however, instead of aerobic exercise they performed light-intensity body conditioning/stretching (eg, flexibility and passive stretching) exercises during which HR was maintained below 40% heart rate reserve (HR typically was kept below 100 beats per minute). No exercise counseling or behavioral change advice was provided; instead, conversations were centered on topics of everyday life (ie, weather, news items, and families). HR and RPE were assessed every 5 minutes. Any placebo intervention must be meaningful, particularly when it requires regular session attendance (and follow-up) for several weeks and when blinding of the intervention is not possible. Participants assigned to exercise-placebo were otherwise asked to continue with their lifestyle as normal. The usual-care group continued with their lives as usual.

Primary Outcome

The primary outcome was differences in QoL as measured by the Functional Assessment of Cancer Therapy–General (FACT-G)[18] at the 8-week follow-up. The Functional Assessment of Cancer Therapy-Breast (FACT-B)[18] was also included. The FACT- G and FACT-B collectively measure five aspects of QoL: physical well-being, functional well-being (FWB), emotional well-being, social/family well-being (SWB), and specific breast cancer concerns (BCS).

Secondary Outcomes

The Revised Piper Fatigue Scale[19] was used to measure fatigue. The satisfaction with life scale[20] was included to assess participants' life as a whole. The Beck Depression Inventory-II[21] was used to assess the severity of depression. The Physical Self-Perception Profile[22] consists of five, six-item subscales: perceived sports competence, attractiveness of body, physical conditioning competence, physical strength competence, and physical self-worth. Physical activity and exercise behavior were assessed by asking participants to consider how often they had participated in one or more physical activities for 20 to 30 minutes per session during their free time in the last 3 months, and by completion of the stage of change for exercise ladder questionnaire (SOC).[23,24]

Aerobic fitness was measured using the submaximal, 8-minute, single-stage walking test[25] performed on a treadmill. Assessments of height, weight, and percentage body fat using bioelectrical impedance analysis were included as indicators of body composition. Measurements of muscle function using a Biodex isokinetic machine (Biodex System 3 Dynamometer; Biodex Medical Systems Inc, Shirley, NY) were also taken (not reported here).

Adherence to the Interventions

Adherence was calculated from session attendance and the amount (duration, RPE, HR) of exercise achieved by participants during sessions was calculated by abstraction from physical activity logs maintained by the researcher.

Baseline Characteristics

At baseline, all participants provided information regarding their medical history specific to their cancer diagnosis. The Index of Multiple Deprivation[26] rank score was calculated for each participant based on residential postcode.

Sample Size Calculations and Statistical Analyses

Power calculations were based on FACT-G as the primary outcome. A pilot study[27] reported a mean difference of 15 units (standard deviation [SD], 15 units) from baseline to 12 weeks follow-up using the FACT-G scale but for a larger trial it seemed more appropriate for us to expect a smaller change of 10 units of FACT-G score between groups. With at least 38 participants in each group (N = 114), the trial would have 80% power at $P < .05$.

Data were analyzed on an intention-to-treat basis. Repeated-measures mixed analysis was used to compare the majority of trial outcomes between the groups at 8- and 24-week follow-up. Treatment alone and in combination with time were considered as fixed effects, with baseline measurement as a covariate, time (8 and 24 weeks) as a repeated factor, and participants as the random factor. Paired comparisons between the groups at each time point were adjusted by the Tukey-Kramer method. The physical activity and SOC data were analyzed with χ^2 tests (with Bonferroni corrections) by comparing the percentages of patients changing physical activity categories to become active at least three times per week and reaching the action or maintenance SOC between the groups over time, respectively. To assess normality of scores, examination of residuals was performed. For those variables that were found to be non-normally distributed, bootstrapping with 1,000 replicates was carried out to assess the reliability of results. The trial statistician was blinded to group codes. Little's test was used to examine whether missing data were missing completely at random.

RESULTS

Trial Participants and Baseline Characteristics

Recruitment took place between January 2003 and July 2005 (Fig 1). The estimated trial recruitment rate of eligible patients was 28.6%.[28] One hundred eight eligible patients were randomly assigned

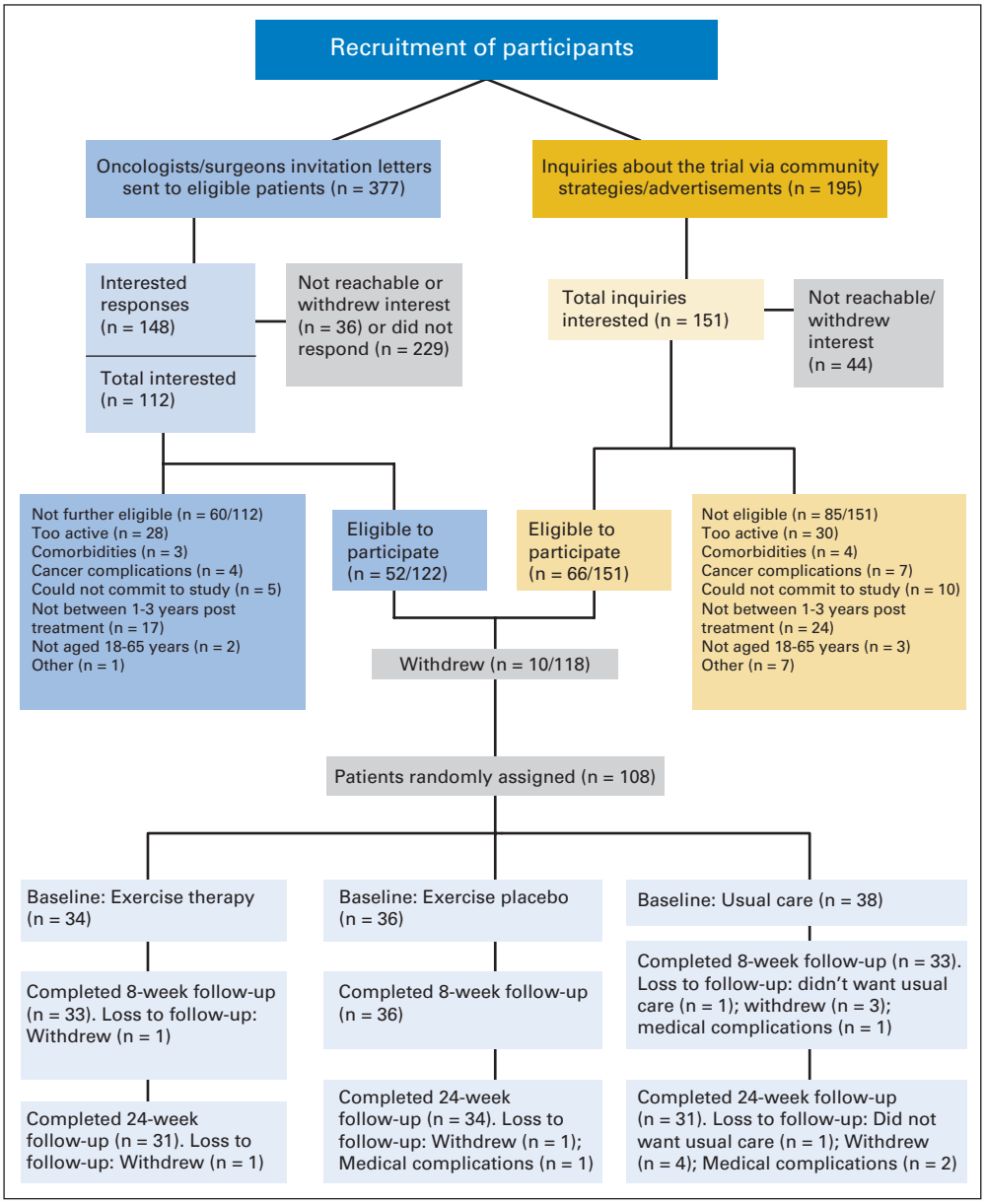

Fig 1. Flow of participants through the trial.

to exercise therapy (n = 34), exercise-placebo (n = 36), or usual care (n = 38). The groups were generally balanced at baseline in relation to demographic, treatment, health behavior, and outcome variables (Tables 1 and 2).

Follow-Up

Follow-up was achieved on 93% of participants at 8-weeks and 89% at 24 weeks. Little's D test indicated that missing data were missing completely at random ($\chi^2 = 88.2$; $df = 1{,}290$; $P = .99$).

QoL Outcomes

Analyses highlighted a significant difference in mean FACT-G scores between exercise therapy and usual-care groups at 8 weeks, favoring exercise therapy (mean difference, 9.8 units; $P = .004$). A significant effect for FACT-B scores was recorded at 8 weeks between exercise therapy and usual care ($P = .002$). A significant (marginal) effect was also seen at 8 weeks between exercise-placebo and usual care ($P = .049$; Fig 2). Significant differences between exercise therapy and usual care at 8 weeks for SWB ($P = .032$), FWB ($P = .014$), and BCS ($P = .038$) were recorded (Table 3).

Psychological Health Outcomes

A significant difference between exercise-placebo and usual care in total fatigue scores at 8 weeks was noted; the usual-care group had higher scores ($P = .037$). A significant mean difference for physical conditioning competence between the exercise therapy and usual-care groups was recorded at both follow-ups, with a reduction in effect at 24 weeks ($P < .01$ in both cases). Analyses also revealed a significant difference in physical self-worth scores between exercise therapy and usual care ($P = .003$) and between exercise-placebo and usual care at 8 weeks ($P = .005$). Significant differences in mean depression scores between exercise therapy and usual care ($P = .001$) and also between exercise-placebo and usual care ($P = .001$) were recorded; usual care

Table 1. Baseline Sociodemographic, Health Behavior, and Cancer Treatment Characteristics

Characteristic	Exercise Therapy (n = 34)		Exercise-Placebo (n = 36)		Usual Care (n = 38)	
	No. of Patients	%	No. of Patients	%	No. of Patients	%
Age, years						
Mean	51.6		50.6		51.1	
SD	8.8		8.7		8.6	
Body mass index, kg/m^2						
Mean	28.5		27.6		29.6	
SD	4.4		4.1		5.1	
Percentage body fat (n = 107)						
Mean	40.2		39.5		41.3	
SD	5.4		6.2		6.1	
Weight, kg (n = 106)						
Mean	77.2		73.9		77.2	
SD	12.1		11.3		14.1	
Aerobic fitness, mL/kg/min (n = 102)						
Mean	29.1		30.3		30.0	
SD	4.8		5.0		5.4	
Smokers	0 of 34	0	5 of 36	13.9	4 of 37	10.9
Ethnicity						
White	34 of 34	100	35 of 36	97.2	37 of 38	97.4
Index of multiple deprivation (n = 107)						
Quartile 1 (least deprived)	9 of 33	27.3	11 of 36	30.6	5 of 38	13.2
Quartile 2	10 of 33	30.3	9 of 36	25.0	12 of 38	31.6
Quartile 3	6 of 33	18.2	11 of 36	30.6	12 of 38	31.6
Quartile 4 (most deprived)	8 of 33	24.2	5 of 36	13.9	9 of 38	23.7
Stage of change for exercise						
Precontemplation/contemplation	16 of 34	47.1	18 of 36	50.0	24 of 36	63.2
Preparation	18 of 34	52.9	18 of 36	50.0	14 of 36	36.8
Previous physical activity						
Never	9 of 34	26.5	9 of 36	25.9	12 of 38	31.6
≤ 3 times per month	7 of 34	20.6	12 of 36	33.3	12 of 38	31.6
Once per week	11 of 34	32.4	9 of 36	25.0	9 of 38	23.7
≥ Twice per week	7 of 34	20.6	6 of 36	16.7	5 of 38	13.2
Employment status						
Employed	26 of 34	76.5	25 of 36	69.4	21 of 34	58.3
Education						
Secondary and A levels	17 of 34	50.0	12 of 35	34.3	18 of 33	54.5
Degree	5 of 34	14.7	13 of 35	37.1	6 of 33	15.2
Other	12 of 34	35.3	10 of 35	28.5	9 of 33	27.2
Marital status						
Married/cohabitating	28 of 34	82.4	31 of 34	86.1	31 of 33	81.6
Single/widowed/divorced	6 of 34	17.6	5 of 34	13.9	7 of 33	18.4
Experiencing lymphoedema	16 of 34	47.0	11 of 36	30.6	18 of 38	47.3
Children	29 of 33	87.9	31 of 35	88.6	30 of 34	88.2
Months post-treatment						
Mean	17.6		18.2		16.7	
SD	7.4		6.9		5.9	
Using hormone therapy	25 of 34	73.5	25 of 36	69.4	29 of 38	76.3
Treated with chemotherapy	27 of 34	79.4	25 of 36	69.4	28 of 38	73.7
Treated with radiotherapy	27 of 34	79.4	28 of 36	77.8	30 of 38	78.9
Treated with surgery						
Mastectomy	18 of 34	52.9	18 of 36	50.0	21 of 38	55.3
Breast-conserving surgery	16 of 34	47.1	18 of 36	50.0	17 of 38	44.7

Abbreviation: SD, standard deviation.

reported higher depression scores. Larger effects were seen at 8 weeks but these benefits persisted at 24 weeks. A significant difference in mean satisfaction with life scores between exercise-placebo and usual care was noted at 24 weeks ($P = .0017$; Table 4).

Physical Health Outcomes and Physical Activity

Evidence of significant differences in aerobic fitness scores were recorded between exercise therapy and usual care ($P = .002$) and exercise-placebo and usual care ($P = .021$) at 8 weeks (Table 4).

Table 2. Baseline Data for Quality-of-Life and Psychological Health Outcomes

Measure	Group					
	Exercise		Exercise-Placebo		Control	
	Mean	SD	Mean	SD	Mean	SD
FACT-G	80.41	13.57	83.57	14.66	80.41	14.76
FACT-B	101.71	18.29	106.03	18.90	101.50	18.35
Physical well-being	23.65	2.97	22.92	3.88	22.21	4.98
Social/family well-being	20.98	5.45	22.49	5.74	20.71	4.74
Emotional well-being	17.12	4.25	17.58	4.57	18.32	3.65
Functional well-being	18.66	6.26	20.58	4.85	19.28	6.00
Breast cancer subscale	21.30	5.91	22.45	5.89	20.88	5.49
Satisfaction with life	4.43	1.42	4.57	1.44	4.89	1.38
Total fatigue	3.25	1.82	3.95	1.92	3.66	1.67
Sport competence	1.57	0.67	1.55	0.56	1.59	0.63
Physical conditioning competence	1.45	0.26	1.54	0.46	1.49	0.52
Attractiveness of body	1.49	0.58	1.55	0.53	1.52	0.55
Physical strength competence	1.55	0.52	1.49	0.39	1.59	0.60
Physical self-worth	1.59	0.46	1.55	0.34	1.63	0.55
Depression	13.56	9.06	11.86	8.01	10.79	7.65

Abbreviations: SD, standard deviation; FACT-G, Functional Assessment of Cancer Therapy–General; FACT-B, Functional Assessment of Cancer Therapy–Breast.

Significant differences in the percentage of participants increasing their physical activity to become active at least three times per week between exercise therapy and usual care were recorded at the 8-week ($P < .001$) and 24-week follow-up ($P < .001$), and also between exercise-placebo and usual care (8 weeks, $P < .001$; 24 weeks, $P = .01$); usual care reported less physical activity. A greater proportion of exercise therapy participants moved to the action or maintenance SOC compared with usual care at 24 weeks ($P < .001$). A similar effect between exercise-placebo and usual care ($P = .03$) was also recorded (Table 5).

Bootstrapping of Trial Outcomes

The variables physical well-being, SWB, satisfaction with life, sport competence, physical conditioning competence, physical appearance, and strength competence were found to have skewed distributions; however, bootstrapping confirmed that *P* values from the mixed-model analysis were stable and therefore correct inferences could be made from the results.

Adherence to the Interventions and Amount of Exercise

Adherence to the interventions was excellent; 77% of the exercise therapy and 88.9% of the exercise-placebo groups, respectively, attended 70% (at least 17 of 24 sessions) or more of sessions. Mean HR for the exercise therapy group ranged from 117.4 (SD, 12.9) to 121.5 (SD, 13.4) throughout the weeks. Mean HR for exercise-placebo ranged from 92.5 (SD, 13.2) to 95.9 (SD, 9.5). Average durations of aerobic exercise achieved by exercise therapy ranged from 25.7 (SD, 6.3) to 27.4 (SD, 6.2) minutes. HR data indicated that both groups were exercising in accordance with the protocol.[13]

DISCUSSION

The primary finding of the study was that a supervised aerobic exercise therapy intervention significantly improved QoL (FACT-G) in previously inactive women treated for breast cancer, relative to usual care. Differences substantially exceeded the minimally important difference[29] of 5 to 6 units for the FACT-G scale at 8 weeks. These findings cannot be attributable to attention effects because the exercise-placebo group did not report significant benefit, compared with usual care. The magnitude of the effect for FACT-G was far greater than those reported for other types of health-enhancing and QoL interventions (eg, psychological support in cancer patients).[30] Furthermore, the efficacy of psychosocial interventions in cancer care has been questioned recently,[31,32] and studies[33] have reported that such interventions do not decrease health care use costs in breast cancer patients; these results strengthen the case for the evaluation of the merits of alternative QoL interventions such as exercise. Given that research has demonstrated that women who engage in exercise decrease their risk of breast cancer reoccurrence,[34] interventions involving exercise take on even greater health importance.

We found significant effects for specific components of QoL; namely SWB, FWB, and BCS, and these generally favored exercise therapy, relative to usual care. These findings are consistent with previous reports[9-10,27] that have found QoL benefits resulting from participation in exercise programs in women undergoing and recovering from breast cancer treatment. The results for FWB are particularly promising, given that physical functioning is considered one of the most important components of QoL in cancer patients.[35] Recent research has reported that high economic costs are associated with functional impairment in breast cancer patients,[36] and participation in regular aerobic exercise may serve to expedite the recovery process. However, we are mindful that this study only demonstrated short-term gains in these outcomes.

Intervention-related improvements in psychological health outcomes were modest but sustained for several end points. The exercise therapy group reported better perceived physical conditioning competence scores than usual care at both follow-ups. Both exercise therapy and exercise-placebo reported higher physical self-worth scores than usual care, but the magnitude of the effect was greater for

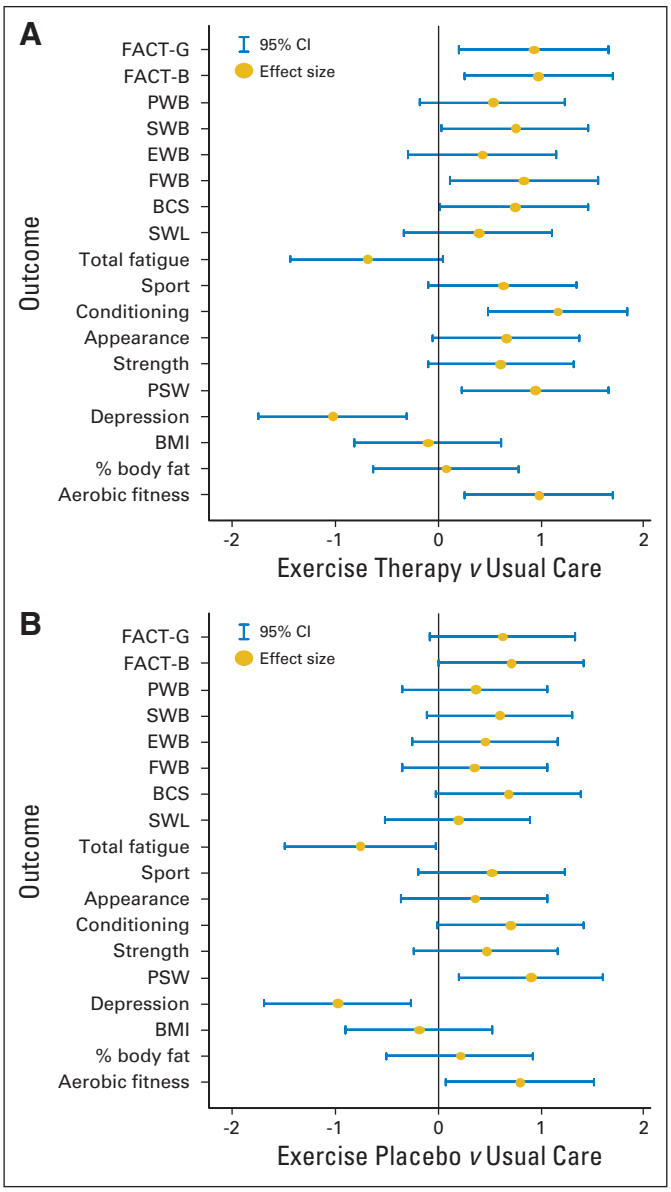

Fig 2. Effect estimates, with 95% confidence intervals, for the difference (adjusted for baseline scores) between (A) exercise therapy versus usual care and (B) exercise-placebo versus usual care at 8-week follow-up. Estimates expressed in units of 1 standard deviation. FACT-G, Functional Assessment of Cancer Therapy–General; FACT-B, Functional Assessment of Cancer Therapy–Breast; PWB, physical well-being; SWB, social/family well-being; EWB, emotional well-being; FWB, functional well-being; BCS, specific breast cancer concerns; SWL, satisfaction with life; PSW, physical self-worth; BMI, body mass index.

exercise therapy. Depression scores were significantly lower in exercise therapy and exercise-placebo compared with usual care at both follow-ups. Only a small benefit for depression beyond the effects of the exercise-placebo condition was noted. We cannot rule out the possibility that light body conditioning and stretching exercises of minimal aerobic exertion also provide psychological benefit to cancer patients; indeed, recent pilot trials[37,38] have suggested that activities such as yoga and tai chi significantly improve psychological well-being in breast cancer patients. Additional research should pursue this issue. We found no group differences for fatigue at follow-up between exercise therapy and usual care, although a difference between exercise-placebo and usual care was noted. These findings are supported by some studies but are inconsistent with others.[9,11]

The nonsignificant findings for body composition outcomes were not surprising, given the short intervention period, and are consistent with systematic review evidence[8] that has indicated no statistically or clinically significant changes in body weight or body mass index in exercise trials involving breast cancer patients. It may be that more direct and accurate assessments (eg, dual x-ray absorptiometry) of body composition are required to be able to detect these outcomes.[39] Although the exercise therapy group demonstrated improved aerobic fitness scores at 8-week follow-up, a significant effect was also seen in the exercise-placebo group, albeit somewhat smaller. There are several possible explanations for this. Given that blinded assessments of outcomes were not a feature of this study, it may be that a Hawthorne effect or a test-retest effect has occurred. It is also possible that the exercise-placebo intervention provided women with aerobic benefit; this explanation seems unlikely, however, given that we know this group worked at less than 40% heart rate reserve. Interestingly, in a trial that compared psychotherapy with psychotherapy plus exercise arms,[9] both groups were found to improve their cardiovascular endurance, highlighting further the importance of including placebo groups in behavioral/lifestyle-based trials.

Exercise therapy and exercise-placebo participants significantly increased their physical activity at both follow-ups, relative to usual care, but the greatest difference was recorded between exercise therapy and usual care. A similar pattern of results was also observed for SOC, with the magnitude of change also larger for exercise therapy than other trial groups. Nevertheless, the data indicated that some intervention contamination had occurred in the exercise-placebo and usual-care groups. To some extent, contamination in the exercise-placebo group was inevitable, given that this group believed they had been assigned to an active exercise arm; consequently, it seems they increased their activity outside of placebo intervention sessions, even though they were asked not to do so. Contamination may also explain the increases in aerobic fitness observed in the exercise-placebo group.

Blinding of the assessments was not possible, although we do not consider this to be a substantial limitation because the primary outcome questionnaire was self-administered. Although the trial was underpowered for the primary outcome, and despite intervention contamination, we were still able to report a significant effect of the magnitude we expected. The low level of attrition across follow-ups was encouraging. This was the first published trial of the benefits of exercise in cancer patients to include both exercise-placebo and usual-care control groups; we regard this was a particular strength over previous studies. Past studies that have examined the effects of exercise interventions in cancer patients generally have failed to provide detailed information about the nature and content of the exercise sessions; without such information it is difficult to know the amount of exercise that is likely to provide benefit to cancer patients. We obtained excellent adherence to the interventions. The study was not statistically powered to detect differences between the intervention groups; therefore, any inferences about such differences should be made with caution until such a trial takes place. Although we adjusted for paired comparisons between groups, there exists the possibility of a type I error due to multiple statistical testing and reported differences

Table 3. Effects of Exercise Therapy and Exercise-Placebo Relative to Usual Care on Quality-of-Life Outcomes (means adjusted for baseline scores)

Quality-of-Life Outcomes		Follow-Up (weeks) 8 Mean Difference	8 95% CI	8 Adjusted *P**	24 Mean Difference	24 95% CI	24 Adjusted *P**
FACT-G	Exercise therapy *v* usual care	**9.80**	2.20 to 17.40	**.004**	7.27	−0.51 to 15.06	.081
	Exercise-placebo *v* usual care	6.62	−0.90 to 14.15	.117	4.72	−2.90 to 12.34	.469
FACT-B	Exercise therapy *v* usual care	**13.14**	3.44 to 22.84	**.002**	8.14	−1.81 to 18.08	.174
	Exercise-placebo *v* usual care	**9.57**	0.04 to 19.10	**.049**	5.89	−3.80 to 15.58	.491
Physical well-being	Exercise therapy *v* usual care	1.69	−0.55 to 3.94	.250	1.09	−1.22 to 3.39	.746
	Exercise-placebo *v* usual care	1.13	−1.07 to 3.33	.667	0.67	−1.59 to 2.92	.955
Social/family well-being	Exercise therapy *v* usual care	**2.58**	0.14 to 5.02	**.032**	1.83	−0.67 to 4.33	.279
	Exercise-placebo *v* usual care	2.06	−0.35 to 4.48	.140	0.81	−1.65 to 3.26	.931
Emotional well-being	Exercise therapy *v* usual care	1.40	−0.95 to 3.74	.513	1.62	−0.79 to 4.02	.376
	Exercise-placebo *v* usual care	1.48	−0.82 to 3.79	.426	1.31	−1.04 to 3.65	.585
Functional well-being	Exercise therapy *v* usual care	**3.71**	0.50 to 6.92	**.014**	2.45	−0.84 to 5.73	.263
	Exercise-placebo *v* usual care	1.58	−1.57 to 4.73	.689	1.85	−1.36 to 5.06	.549
Breast cancer subscale	Exercise therapy *v* usual care	**3.37**	0.12 to 6.61	**.038**	1.60	−1.72 to 4.91	.727
	Exercise-placebo *v* usual care	3.06	−0.11 to 6.24	.065	1.79	−1.46 to 5.03	.599

NOTE. Bold font indicates variables where significant differences exist between the groups and *P* values.
Abbreviations: FACT-G, Functional Assessment of Cancer Therapy-General; FACT-B, Functional Assessment of Cancer Therapy-Breast.
*Paired comparisons between groups at each time point were adjusted by the Tukey-Kramer method.

may be spurious, but the consistent trends toward benefit for exercise therapy suggests differences, where identified, are real. Use of the same researcher in both interventions subjected the study to potential intervener expectancy effects.

In summary, in women treated for breast cancer in the United Kingdom, we report large, clinically important, short-term benefits in QoL from participation in exercise therapy. Longer term effects in a number of other outcomes were also found, relative to usual care.

Table 4. Effects of Exercise Therapy and Exercise-Placebo on Psychological and Physical Health Outcomes (means adjusted for baseline scores)

Psychological and Physical Health Outcomes		Follow-Up (weeks) 8 Mean Difference	8 95% CI	8 Adjusted *P**	24 Mean Difference	24 95% CI	24 Adjusted *P**
Total fatigue	Exercise therapy *v* usual care	−1.13	−2.36 to 0.09	.085	−0.68	−2.04 to 0.68	.694
	Exercise-placebo *v* usual care	**−1.25**	−2.44 to −0.05	**.037**	−1.15	−2.48 to 0.18	.128
Sports competence	Exercise therapy *v* usual care	0.29	−0.04 to 0.62	.124	0.19	−0.15 to 0.52	.604
	Exercise-placebo *v* usual care	0.24	−0.09 to 0.57	.285	0.22	−0.11 to 0.56	.382
Physical conditioning competence	Exercise therapy *v* usual care	**0.60**	0.25 to 0.96	**< .001**	**0.46**	0.11 to 0.82	**.004**
	Exercise-placebo *v* usual care	0.34	−0.00 to 0.69	.054	0.33	−0.02 to 0.68	.081
Attractiveness of body	Exercise therapy *v* usual care	0.28	−0.02 to 0.59	.086	0.27	−0.04 to 0.58	.132
	Exercise-placebo *v* usual care	0.15	−0.15 to 0.46	.693	0.20	−0.11 to 0.50	.425
Physical strength competence	Exercise therapy *v* usual care	0.32	−0.05 to 0.68	.131	0.33	−0.04 to 0.71	.117
	Exercise-placebo *v* usual care	0.24	−0.12 to 0.61	.373	0.26	−0.11 to 0.62	.313
Physical self-worth	Exercise therapy *v* usual care	**0.49**	0.12 to 0.86	**.003**	0.27	−0.10 to 0.65	.286
	Exercise-placebo *v* usual care	**0.47**	0.10 to 0.83	**.005**	0.35	−0.02 to 0.72	.069
Depression	Exercise therapy *v* usual care	**−6.01**	−10.21 to −1.81	**.001**	**−4.49**	−8.78 to −0.20	**.035**
	Exercise-placebo *v* usual care	**−5.66**	−9.76 to −1.55	**.001**	**−4.98**	−9.14 to −0.81	**.009**
Satisfaction with life	Exercise therapy *v* usual care	0.72	−0.61 to 2.04	.617	0.98	−0.38 to 2.35	.2985
	Exercise-placebo *v* usual care	0.35	−0.94 to 1.65	.967	1.83	0.50 to 3.15	**.0017**
Percentage body fat	Exercise therapy *v* usual care	0.24	−1.94 to 2.41	.999	−0.33	−2.67 to 2.01	.998
	Exercise-placebo *v* usual care	0.64	−1.48 to 2.76	.951	−0.75	−3.01 to 1.50	.927
Body mass index	Exercise therapy *v* usual care	−0.09	−0.75 to 0.57	.999	−0.03	−0.72 to 0.65	.999
	Exercise-placebo *v* usual care	−0.17	−0.81 to 0.48	.975	−0.30	−0.97 to 0.37	.791
Aerobic fitness	Exercise therapy *v* usual care	**2.89**	0.78 to 4.99	**.002**	1.24	−0.98 to 3.45	.583
	Exercise-placebo *v* usual care	**2.25**	0.22 to 4.28	**.021**	0.98	−1.16 to 3.13	.761

NOTE. Bold font indicates variables where significant differences exist between the groups and *P* values.
*Paired comparisons between groups at each time point were adjusted by the Tukey-Kramer method.

Table 5. Intervention Effects Upon Physical Activity and Stage of Change for Exercise

Intervention	Follow-Up (weeks) 8 No. of Patients	8 %	24 No. of Patients	24 %
Physical activity*				
Aerobic exercise therapy	27 of 33	82	18 of 31	58
Exercise-placebo	23 of 36	64	12 of 34	35
Usual care	3 of 35	9	3 of 36	8
Stage of change for exercise†				
Aerobic exercise therapy	—		16 of 31	52
Exercise-placebo	—		10 of 34	29
Usual care	—		2 of 31	6

*Analyses were performed comparing the percentages of patients that reported a change from being inactive at baseline (ie, never, once per month, 2 to 3 times per month, once per week, and two times per week categories) to being active at least three times per week at follow-up between the groups.
†Stage of change for exercise is not reported at 8-week follow-up because this measure assesses behavior change over a period of 6 months. Analyses were performed comparing the percentages of patients that reported a change from being at risk (ie, precontemplation, contemplation, and preparation) at baseline to being in the action or maintenance stages of change at follow-up between the groups.

Attention effects do not appear responsible for the QoL benefits associated with participation in aerobic exercise in this population, but researchers should consider the possibility that attention effects, at least in part, are responsible for some of the psychological benefits experienced by cancer patients who engage in exercise programs.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The authors indicated no potential conflicts of interest.

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