

**WHAT IS ALREADY KNOWN ON THIS TOPIC**

Antithyroid drugs are often used before, during, or after radioiodine treatment for hyperthyroidism

There is still disagreement about the overall beneficial and detrimental effects and the optimal sequencing of the different antithyroid drugs before or after radioiodine treatment

**WHAT THIS STUDY ADDS**

Adjunctive antithyroid drugs reduce the biochemical exacerbation of hyperthyroidism directly after radioiodine treatment

When given in the week before or after radioiodine, antithyroid drugs increase the failure rates and reduce the hypothyroidism rates

This meta-analysis, in contrast with the conclusions of most single trials, suggests that antithyroid drugs increase rates of failure and reduce rates of hypothyroidism when they are given in the week before or after radioiodine treatment. Results from trials included in this review, however, do not allow us to draw firm conclusions regarding the optimal interruption period of antithyroid drugs for patients undergoing radioiodine treatment to avoid both relapse of hyperthyroidism and cardiovascular complications while keeping the long term risk of hypothyroidism at an acceptable level.

Adequately powered randomised long term follow-up trials are needed to examine a potential superiority of longer discontinuation intervals.

We thank Peter Wolf for assistance in electronic libraries search and Liu Kun, Sibylle Tschumi, and Martin Stoecklin for translations. We also thank Marcel Wolbers for statistical advice and Helmut Rasch and Anthony Toft for their valuable comments on the manuscript.

**Contributors:** See bmj.com.

**Funding:** MB and HCB are supported by grants from santésuisse and the Gottfried and Julia Bangerter-Rhyner-Foundation.

**Competing interests:** None declared.

**Ethical approval:** Not needed.

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Accepted: 4 January 2007

## Benefits of supervised group exercise programme for women being treated for early stage breast cancer: pragmatic randomised controlled trial

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BMJ 2007;334:517-20

doi: 10.1136/bmj.39094.648553.AE

**ABSTRACT**

**Objectives** To determine functional and psychological benefits of a 12 week supervised group exercise programme during treatment for early stage breast cancer, with six month follow-up.

**Design** Pragmatic randomised controlled prospective open trial.

**Setting** Three National Health Service oncology clinics in Scotland and community exercise facilities.

**Participants** 203 women entered the study; 177 completed the six month follow-up.

**Interventions** Supervised 12 week group exercise programme in addition to usual care, compared with usual care.

**Main outcome measures** Functional assessment of cancer therapy (FACT) questionnaire, Beck depression inventory, positive and negative affect scale, body mass index, seven day recall of physical activity, 12 minute walk test, and assessment of shoulder mobility.

**Results** Mixed effects models with adjustment for baseline values, study site, treatment at baseline, and age gave intervention effect estimates (intervention minus control) at 12 weeks of 129 (95% confidence interval 83 to 176) for

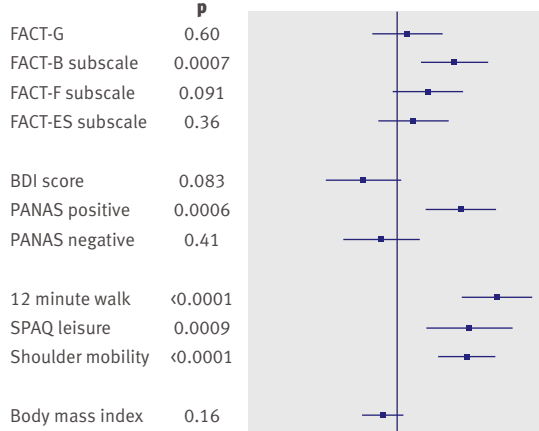
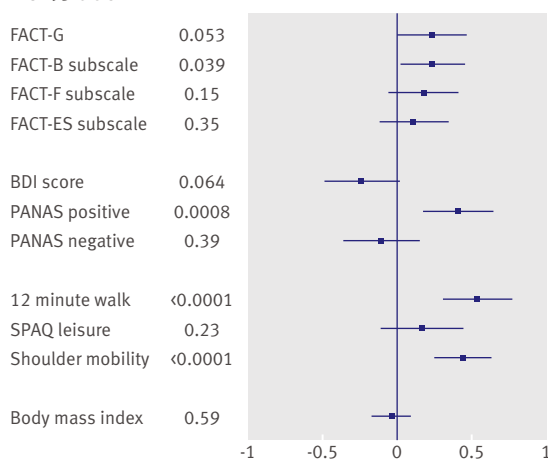
metres walked in 12 minutes, 182 (75 to 289) for minutes of moderate intensity activity reported in a week, 2.6 (1.6 to 3.7) for shoulder mobility, 2.5 (1.0 to 3.9) for breast cancer specific subscale of quality of life, and 4.0 (1.8 to 6.3) for positive mood. No significant effect was seen for general quality of life (FACT-G), which was the primary outcome. At the six month follow-up, most of these effects were maintained and an intervention effect for breast cancer specific quality of life emerged. No adverse effects were noted.

**Conclusion** Supervised group exercise provided functional and psychological benefit after a 12 week intervention and six months later. Clinicians should encourage activity for their patients. Policy makers should consider the inclusion of exercise opportunities in cancer rehabilitation services.

**Trial registration** Current controlled trials ISRCTN12587864.

**INTRODUCTION**

Treatments for cancer can result in significant reductions in many different quality of life outcomes.<sup>1</sup> Current programmes in cancer rehabilitation are mainly based on psychotherapy or social support. Such

**Effect estimates at 12 weeks (exercise–control, in units of 1 SD) with 95% CIs****Effect estimates at 6 months (exercise–control, in units of 1 SD) with 95% CIs**

Effect estimates (intervention minus control), with 95% confidence intervals and P values, for outcome variables at the 12 week assessment (top) and the six month follow-up assessment (bottom), expressed in units of one standard deviation (SD) of the outcome distributions, based on mixed effects models with adjustment for baseline values, study site, treatment at baseline, and age. BDI=Beck depression inventory; FACT=functional assessment of cancer therapy (see text for subscales); PANAS=positive and negative affect scale; SPAQ=Scottish physical activity questionnaire

therapies do not deal with the physical problems encountered by patients, such as fatigue, loss of functional capacity, and weight gain.<sup>2</sup> Exercise is an intervention that may improve a range of quality of life problems after diagnosis of cancer.

Physical activity levels reduce significantly for many women after a diagnosis of breast cancer and remain low after treatment is completed.<sup>3 4</sup> A recent systematic review of the effects of exercise on breast cancer patients and survivors concluded that exercise is an effective intervention to improve quality of life, cardiorespiratory fitness, physical functioning, and fatigue.<sup>5</sup>

We aimed to determine if participating in a supervised group exercise programme for women during treatment for early stage breast cancer had functional

and psychological benefits. We tested the hypotheses that 12 weeks of supervised group exercise would improve quality of life for women during treatment for early stage breast cancer and that benefits would be maintained for six months after the intervention.

**METHODS**

**Participants**—From January 2004 to January 2005, we recruited women with stage 0-III breast cancer at outpatient clinics for chemotherapy or radiotherapy at three National Health Service oncology centres in Scotland.<sup>6</sup> Exclusion criteria were concurrent unstable cardiac, hypertensive, or respiratory disease; cognitive dysfunction; and regular exercise.

**Protocol, assignment, and masking**—We randomly allocated women into one of two groups. The randomisation was stratified by hospital and treatment at baseline (chemotherapy, radiotherapy, or combination). The study was a pragmatic, randomised, controlled, prospective, open trial. We took steps to blind the evaluation of outcomes.

**Outcome measures**—The primary outcome measure was quality of life, as measured by the functional assessment of cancer therapy—general (FACT-G) questionnaire.<sup>7</sup> Secondary outcomes were the specific subscales of the FACT-G (breast cancer, FACT-B; fatigue, FACT-F; and endocrine symptoms, FACT-ES), Beck depression inventory, positive and negative affect scale, body mass index, seven day recall of physical activity, performance in a 12 minute walk test, and score on a shoulder mobility test.<sup>8-12</sup>

**Intervention**—Women assigned to the intervention group received usual care from their healthcare team and attended a supervised group exercise programme. The exercise programme ran for 12 weeks, and women were encouraged to attend two classes and do one additional exercise session at home each week. The exercise intervention was based on guidelines for prescription of exercise for cancer patients and survivors.<sup>13</sup> At the end of the 12 week intervention, the women were helped to construct an individual exercise programme. Further details of the intervention and the expertise of the staff are available on our website ([www.strath.ac.uk/sca/staff/mutrie\\_n.html](http://www.strath.ac.uk/sca/staff/mutrie_n.html)). Women assigned to the control group received usual care from the healthcare team and completed all outcome measures on the same time frame as the intervention group.

**Statistical analysis**—We tested whether significant differences existed between the exercise group and control group in all outcomes at the end of the 12 week intervention period and at six months post-intervention, adjusting for the stratification variables (study site and treatment at baseline), age, and baseline value of the outcome. We did the analysis on an intention to treat basis.

**RESULTS****Participants**

The recruiters approached 1144 women, and 313 agreed to attend pre-screening. We randomised 203

women. The women were recruited on average six months after diagnosis, had a mean age of just over 50, and came from a range of occupations. No obvious imbalances existed between study groups (see *bmj.com*).

### Main outcomes

The table summarises the outcome variables measured at the baseline, 12 week, and six month post-intervention assessments, for the intervention and control groups separately. The figure shows effect estimates and confidence intervals for all variables.

Mixed effects models with adjustment for baseline values, study site, treatment at baseline, and age showed intervention effect estimates (intervention minus control) at 12 weeks of 129 (95% confidence interval 83 to 176) for metres walked in 12 minutes, 182 (75 to 289) for minutes of moderate intensity activity reported in a week, 2.6 (1.6 to 3.7) for shoulder mobility, 2.5 (1.0 to 3.9) for breast cancer specific subscale quality of life, and 4.0 (1.8 to 6.3) for positive mood. We found no significant intervention effect for FACT-G, which was the primary outcome. We saw non-significant trends towards increases in perceived quality of life in relation to fatigue (+2.3 points,  $P=0.091$ ) and reduced depression (-1.7 points,  $P=0.083$ ) in favour of the intervention.

Intervention effect estimates for the six month follow-up data were 105 (60 to 151) for metres walked in 12 minutes, 2.5 (1.4 to 3.6) for shoulder mobility, 1.5 (0.1 to 2.9) for breast cancer specific subscale quality of life (when this subscale is added to the FACT-G a significant effect (4.9, 0.2 to 9.6) for FACT-B emerges), and 3.9 (1.6 to 6.1) for positive mood. The intervention group reported fewer nights in hospital (Mann-Whitney test,  $P=0.044$ ) and fewer visits to their general practitioner ( $P=0.011$ ) than the control group.

Outcome variables and intervention effect estimates (95% confidence intervals) with P values\*

Outcome variable	Mean (SD)			Effect estimates (exercise-control)	
	Baseline	12 weeks	6 months	12 weeks	6 months
<b>Maximum No:</b>					
Control	102	92	95		
Exercise	99	82	82	NA	NA
<b>FACT-G:</b>					
Control	73.3 (15.0)	77.3 (14.4)	77.1 (17.0)	1.0 (-2.7 to 4.7);	3.6 (0.0 to 7.3);
Exercise	77.0 (12.4)	81.0 (16.8)	83.2 (12.8)	$P=0.60$	$P=0.053$
<b>FACT-B subscale:</b>					
Control	21.3 (7.0)	22.4 (7.2)	24.2 (6.3)	2.5 (1.0 to 3.9);	1.5 (0.1 to 2.9);
Exercise	22.2 (6.7)	25.8 (6.0)	26.1 (5.6)	$P=0.0007$	$P=0.039$
<b>FACT-F subscale:</b>					
Control	32.8 (12.7)	36.0 (12.1)	37.6 (11.8)	2.3 (-0.4 to 5.0);	1.9 (-0.7 to 4.6);
Exercise	36.3 (11.7)	40.3 (10.4)	41.3 (9.7)	$P=0.091$	$P=0.15$
<b>FACT-ES subscale:</b>					
Control	39.9 (9.3)	40.3 (9.7)	39.7 (10.2)	1.1 (-1.2 to 3.4);	1.1 (-1.2 to 3.4);
Exercise	40.6 (9.6)	41.6 (9.1)	41.0 (9.8)	$P=0.36$	$P=0.35$
<b>BDI score:</b>					
Control	13.0 (7.4)	11.5 (8.6)	10.8 (7.5)	-1.7 (-3.7 to 0.2);	-1.8 (-3.8 to 0.1);
Exercise	11.8 (6.9)	8.6 (6.8)	8.4 (7.2)	$P=0.083$	$P=0.064$
<b>PANAS positive:</b>					
Control	28.0 (9.2)	29.3 (9.8)	29.2 (10.5)	4.0 (1.8 to 6.3);	3.9 (1.6 to 6.1);
Exercise	27.7 (8.4)	33.4 (8.5)	33.0 (8.1)	$P=0.0005$	$P=0.0008$
<b>PANAS negative:</b>					
Control	19.1 (7.7)	17.7 (7.4)	17.4 (6.9)	-0.7 (-2.5 to 1.0);	-0.7 (-2.5 to 1.0);
Exercise	17.3 (6.9)	15.6 (6.6)	15.7 (6.1)	$P=0.41$	$P=0.39$
<b>12 minute walk (m):</b>					
Control	975 (235)	984 (221)	1013 (190)	129 (83 to 176);	105 (60 to 151);
Exercise	997 (211)	1135 (143)	1127 (166)	$P<0.0001$	$P<0.0001$
<b>SPAQ leisure activity (minutes):</b>					
Control	365 (288)	416 (405)	427 (370)	182 (75 to 289);	64 (-41 to 169);
Exercise	367 (306)	585 (385)	492 (327)	$P=0.0009$	$P=0.23$
<b>Shoulder mobility score:</b>					
Control	30.5 (5.6)	30.1 (5.9)	29.6 (6.2)	2.6 (1.6 to 3.7);	2.5 (1.4 to 3.6);
Exercise	31.1 (5.4)	33.2 (4.6)	32.8 (4.8)	$P<0.0001$	$P<0.0001$
<b>Body mass index:</b>					
Control	27.5 (6.0)	27.9 (6.9)	27.0 (5.4)	-0.5 (-1.3 to 0.2);	-0.2 (-0.9 to 0.5);
Exercise	27.3 (5.2)	26.9 (4.3)	27.0 (4.6)	$P=0.16$	$P=0.59$

BDI=Beck depression inventory; FACT=functional assessment of cancer therapy (see text for subscales); NA=not applicable; PANAS=positive and negative affect scale; SPAQ=Scottish physical activity questionnaire.

\*Based on mixed effects models with adjustment for baseline values, study site, treatment at baseline, and age.

**WHAT IS ALREADY KNOWN ON THIS TOPIC**

Exercise has a large potential to improve physical and psychosocial aspects of quality of life in women with breast cancer during and after treatment

Most studies have involved home based or individualised gym based exercise programmes

None of the existing evidence comes from the UK or a National Health Service setting

**WHAT THIS STUDY ADDS**

Supervised group exercise provided functional and psychological benefits in both the short term and long term for women having treatment for breast cancer

Clinicians should encourage physical activity for patients, and policy makers should consider including exercise opportunities in cancer rehabilitation services

**DISCUSSION****Principal findings**

After 12 weeks of supervised exercise, the intervention group showed benefits in physical and psychological functioning in comparison with the control group. No adverse events were reported. The benefits to the intervention group reported at 12 weeks were maintained to the six month follow-up, with the exception of self reported minutes of physical activity. The benefits to breast cancer specific quality of life (FACT-B) from the intervention emerged only at the six month follow-up, when most women were post-treatment.

**Strengths and weaknesses**

This is the first full scale randomised controlled trial in the United Kingdom of a group based exercise programme for breast cancer patients during treatment and has the largest sample size of published exercise trials in breast cancer. The study had an appropriate range and number of participants and is unique in including a follow-up. The dropout rate from the trial was 14%, which is similar to other studies on exercise in cancer.<sup>14</sup>

One weakness is that we do not know which aspect of the group exercise experience provided most benefit. Our qualitative data suggest that the group itself was an important aspect and that exercise in standard settings did not provide the same benefits.<sup>15</sup> However, studies that have used appropriate comparison groups to rule out a placebo effect suggest that these beneficial effects cannot be completely attributed to non-specific characteristics of the programme.<sup>16,17</sup> In addition, improvements in the 12 minute walk and shoulder mobility tests in favour of the intervention group are more directly attributable to the exercise than to the group effect.

**Meaning**

A diagnosis of cancer can signal a “teachable moment,” and patients often show an enhanced motivation to change lifestyle behaviours.<sup>18</sup> Clinicians

should encourage activity for patients with cancer, and policy makers should consider including opportunities for exercise in cancer rehabilitation services. Further research is needed on the effects of exercise on patients with and survivors of cancers other than breast cancer. Home based programmes need to be evaluated.

**Conclusion**

Supervised group exercise in addition to usual care for women receiving treatment for early stage breast cancer provided functional and psychological benefit at the end of a 12 week programme and at the six month follow-up.

**Contributors:** See bmj.com.

**Funding:** Cancer Research UK. The funders were independent from the conduct and outcomes of this study. CE is funded by the UK Medical Research Council.

**Competing interests:** None declared.

**Ethical approval:** West ethics committee of Greater Glasgow Health Board (LREC Ref:03/22(2)).

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Accepted: 26 December 2006