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Exercise therapy in women treated for breast cancer

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ABSTRACT

Treatment for breast cancer can result in reduced quality of life (QoL), psychological and physical well-being. Evidence suggests that exercise may be of therapeutic benefit for breast cancer patients. To date, however, no randomised controlled trial in the UK has examined the effects of aerobic exercise therapy upon QoL and associated outcomes in women who have completed breast cancer treatment. Furthermore no trial has included an exercise-placebo and a usual care group to control for possible attention effects arising from instructor-patient interaction. Therefore, the purpose of this thesis was to examine the effects of a supervised one-to-one aerobic exercise-therapy intervention upon QoL and associated outcomes in women who had completed treatment for breast cancer 12-36 months previously. Additional aims of the thesis were to provide detailed information about participants' adherence to the trial interventions and to examine the most effective methods of recruitment into the trial. A qualitative study was also included to explore the personal exercise experiences of participants who took part in the exercise therapy and exercise-placebo interventions.

The sample consisted of 108 sedentary women who had been treated for breast cancer 12-36 months previously. The mean age of the participants was 51 years (age range 32-65years). The primary route of recruitment was via clinician invitation letters. Participants were randomised to one of three groups: exercise therapy (n=34), exercise-placebo (n=36) or usual care (n=38). The exercise therapy and exercise-placebo groups attended one-to-one supervised sessions three times a week for a period of eight weeks (24 sessions in total). The exercise therapy group participated in moderate intensity aerobic exercise and received exercise counselling designed to promote exercise participation. The exercise-placebo group participated in light flexibility, mobility and body conditioning exercises and did not receive exercise counselling.

Repeated measures mixed analyses of covariance (controlling for baseline scores) revealed a significant mean difference of 9.8 units in the primary outcome (QoL), Functional Assessment of Cancer Therapy (FACT-G)-General scale, favouring exercise therapy at eight week follow-up relative to usual care. The exercise placebo group did not report similar statistical significant benefits. Significant differences favouring exercise therapy relative to usual care were found for FACT-B (breast cancer specific QoL), social/family well-being, functional well-being and breast specific concerns subscales. Outcomes including depression, physical self-worth and aerobic fitness improved significantly in the exercise therapy group compared to usual care. Adherence to both exercise interventions was excellent. The estimated trial recruitment rate based on clinician invitation was 28.6%.

Findings from the qualitative study revealed participants perceived the exercise interventions had accelerated their psychological and physical recovery from breast cancer. A patient-centred approach mediated exercise enjoyment and adherence.

This pioneering study demonstrated that exercise therapy was a safe, tolerable intervention that elicited short-term, clinically important benefits upon QoL in women treated for breast cancer. Future research should focus on sustaining QoL benefits through longer-term exercise participation and the feasibility of integrating exercise rehabilitation into mainstream breast cancer care.

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PEER REVIEWED MATERIAL FROM THIS THESIS

Publications

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Daley, A.J., Crank, H., Mutrie, N., Saxton, J., Coleman, R. Patient recruitment into a randomised controlled trial of supervised exercise therapy in sedentary women treated for breast cancer. *Contemporary Clinical Trials.*2007;28(5):603-13.

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Daley, A.J., Mutrie, N., Crank, H., Coleman, R., Saxton, J. Exercise therapy in women who have had breast cancer: Design of the Sheffield women's exercise and well-being project. *Health Education Research.* 2004; 19(6):686-697.

CANDIDATE'S STATEMENT

A research grant was awarded to Dr. Amanda Daley from Cancer Research UK to investigate the effects of exercise upon quality of life and psychological well-being in women treated for breast cancer. The PhD candidate was responsible for translating and developing the initial trial outline into a randomised controlled trial. Activities included trial promotion, recruitment of participants, liaising with collaborating health professionals, management of a recruitment database, pre-study familiarisation and participant medical screening. A significant contribution to the trial was the design and delivery of the exercise therapy and exercise-placebo interventions. To enhance intervention delivery the candidate undertook a residential exercise and cancer rehabilitation certification course to further her cancer-specific exercise knowledge. Exercise sessions and assessment of outcomes were delivered and undertaken by the candidate. This involved over 2000 hours of patient contact time. Additionally the candidate was responsible for data collection and entry; questionnaire data entry was assisted by Mrs. Paula Saxton and data cleaning was performed jointly by the candidate and Dr. Daley. Quantitative data analysis and interpretation was undertaken with Dr. Daley and Ms. Andrea Roalfe; the trial statistician. The candidate assisted with the writing, proof reading and production of journal manuscripts. A qualitative study which investigated the experiences of the participants in the exercise trial intervention groups was conceived and carried out by the candidate. All data collection and transcription of interview data was performed by the candidate. Qualitative data analysis was assisted by Mrs. Sue Kesterton and Dr. Rob Copeland.

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LIST OF ABBREVIATIONS

The following abbreviations are referred to in this thesis;

RCT	Randomised Controlled Trial
QoL	Quality of Life
FACT-G	Functional Assessment of Cancer Therapy - General
FACT-B	Functional Assessment of Cancer Therapy - Breast
PWB	Physical well-being
SWB	Social well-being
EWB	Emotional well-being
FWB	Functional well-being
BCS	Breast cancer subscale
PSPP	Physical Self-Perception Profile
BDI -II	Beck Depression Inventory II
SWL	Satisfaction With Life scale
TPB	Theory of Planned Behaviour
PSW	Physical self-worth
PBC	Perceived Behavioural Control
SOC	Stage of change for exercise
TTM	Transtheoretical Model
IMD	Index of Multiple Deprivation
BMI	Body Mass Index
VO_2 max	(Estimated) Maximal oxygen capacity
HR	Heart-rate
RPE	Rate of perceived exertion
Ex	Exercise therapy participant
E-P	Exercise-placebo participant

CHAPTER 1.0 INTRODUCTION

1.1 INCIDENCE OF BREAST CANCER

Worldwide, the incidence of breast cancer in women has been rising. The highest recorded incidence rates are in the United States of America (USA) and other western developed countries. Rates in Japan, India and China are a quarter of those in the USA.[1] Breast cancer is the most common cancer in women in the United Kingdom (UK) (excluding non-melanoma skin cancer). According to the Office for National Statistics [2] 43,756 new cases were diagnosed in the U.K. in 2003. Breast cancer accounts for nearly 30% of all cancers in women in the UK.[3] There is an underlying trend for an increase in breast cancer in women between 45-99 years in the UK.[4] This observation is supported by the rise in age standardised rate per 100,000 population, which increased from 79 in 1980 to 117 in 1999.[5] Furthermore, the age-standardised incidence in the UK is among the highest in the world. It is estimated that in the UK one in nine women will develop breast cancer at some time during their life. Thus, the lifetime risk is almost 11%.[6]

1.2 BREAST CANCER MORTALITY AND SURVIVAL

Survival rates vary depending upon the biological characteristics and stage of the breast tumour. This is inclusive of size of tumour, presence of metastases in the axillary nodes and the presence of distant metastases of the tumour when it is diagnosed.[1] Women who are diagnosed with early-stage breast cancer and thus have absence of metastatic spread to the axillary nodes, have a better relative survival than women who are diagnosed with more advanced disease. Survival for women with breast cancer has improved significantly. In the early 1970's the five-year relative survival rates were approximately 55% and this figure has steadily risen to 74% for the period

1991–1993.[7] The five-year relative survival rate in the Trent health region, (based on the latest diagnosis period 1991–1995), shows that the highest survival rate is achieved by those patients in the 55-64 years group at 80.8%.[8] The younger age groups <45 years and the older age groups >65 years have a less favourable five-year relative survival rate.

Breast cancer is the second most common cause of cancer death (after lung cancer) of women in the UK.[6] In 1999 there were 11,500 deaths from breast cancer in England and Wales, equating to 18% of all female cancer deaths.[7] Despite increasing incidence rates the number of deaths have fallen since the late 1980's.[9] Mortality in the 1990's will have been directly affected by screening, the widespread use of the drug Tamoxifen, improvements in chemotherapy treatment and improved provision of cancer services.[10] Although the incidence of breast cancer is high, survival is good compared to other cancers; it is estimated that there are approximately 172,000 women alive in the UK who have been diagnosed with breast cancer in the last ten years.[11]

1.3 AETIOLOGY OF BREAST CANCER

Breast cancer is a malignant, metastasising cancer of the mammary gland.[12] An increasing number of cancers are of the pre-invasive form known as ductal carcinoma in situ and lobular carcinoma in situ (These forms of breast cancer essentially do not have a metastatic potential at this stage of diagnosis). Invasive or infiltrating cancer refers to cancer cells that have started to break through normal breast tissue barriers and invade surrounding areas. Invasive cancers can spread cancer to other parts of the body through the bloodstream and lymphatic system. The lymph nodes may be affected first. Invasive ductal carcinoma in situ is the most common cell type accounting for 70-80% of all cases.[13] The appropriate treatment for breast cancer and the prognosis depends upon

the evaluation of the tumour. This is achieved by two types of evaluation; grading and staging. The most commonly used classification to determine the extent and progression of the cancer is the TNM (tumour-node-metastasis) four stage classification system.[14] This system is used to determine the extent and progression of cancer. The higher the stage the further the cancer has progressed. The therapeutic management of breast cancer is partly formulated on the basis of TNM staging. Further examination of the tumour will reveal the estrogen-receptor (ER) and progesterone–receptor (PR) protein status of the primary tumour. The female hormone estrogen is a major factor in the growth of many breast cancers.[15] Cells that are hormone sensitive are easier to treat than cells that lack hormone receptors.

1.4 BREAST CANCER TREATMENT AND RELATED SIDE-EFFECTS

The goal of treatment is to achieve remission whereby the tumour ceases to grow or decreases in size.[16] The treatment of breast cancer often involves a multi-modal treatment approach; a combination of surgery, chemotherapy, radiotherapy and hormonal therapy are employed in the management of breast cancer. Breast cancer patients face a diversity of physical and emotional sequelae of breast cancer treatment.[17-19] The physical side effects from surgery, chemotherapy, radiotherapy and hormonal therapy may include fatigue and weight gain, asthenia, ataxia, reduced cardiovascular function, muscle weakness, atrophy, difficulty sleeping, nausea, vomiting, pain, osteoporosis, lymphoedema and reduced capacity to exercise.[16,20-22] A lower level of physiological functioning has been reported in breast cancer patients post treatment.[23] Common psychological and emotional sequelae of cancer diagnosis and treatment may include depression, anxiety, stress, decreased self-esteem, body image concerns, social isolation and loss of sense of control and the fear of cancer recurrence.[24-27] Thus, quality of life (QoL) can be adversely affected by the cancer

experience and treatment effects.[17,19,28] Pinto and colleagues [29] have suggested that the psychological and physiological responses to breast cancer diagnosis and treatment are likely to be responsible for impacting upon breast cancer patients other health behaviours.

Long periods of inactivity due to treatment regimes and convalescence may further compound physiological and psychological well-being, resulting in reduced cardiovascular function, reduced pulmonary function, reduced range of arm motion, decreased strength, deterioration of lean body tissue and changes in weight and body composition and sleep disturbance.[30-34]

Jacobsen and Stein, [35] and Mock [36] report that persistent fatigue is a long-term debilitating side effect in breast cancer patients following adjuvant chemotherapy or radiation therapy. This finding is supported by recent research by Bower and colleagues who conclude that 34% of breast cancer patients were still experiencing significant fatigue 5-10 years after diagnosis.[37] Interestingly, this type of chronic fatigue is not alleviated by rest, [38,39] posing the question as to the optimal management of one of the symptoms affecting breast cancer patients. Further, Piper [40] found that women who were receiving treatment for breast cancer felt that changes in their psychological well-being status inclusive of stress, worry, depression and anxiety were the main determinants responsible for their feelings of fatigue. Indeed the prevalence of depression in cancer patients is estimated to be two to three times higher than in the general population.[41] Fatigue is a recognised symptom of depression in women with breast cancer.[42] Either by itself or through secondary links with depression is or reduced physical well-being fatigue is a significant symptom for cancer patients.[43] Although it seems apparent there are several contributing factors, it would appear that

fatigue is amenable to exercise based interventions.[44-49] For example, recent research by Mock et al [36] found that women who were undergoing chemotherapy or radiation therapy who adhered to a home-based moderate intensity walking programme for the duration of their treatment significantly reduced their levels of fatigue. Evidence to date suggests that cancer patients should be encouraged to maintain an optimum level of physical activity during and post-cancer treatment to mediate the effects of cancer related fatigue.[50]

1.5 RISK FACTORS FOR BREAST CANCER

The aetiology of breast cancer is multi-factorial and it is likely that breast cancer risk is attributable to a combination of factors rather than one in isolation. Risk factors fall into two categories; modifiable and non-modifiable. The strongest risk factor for breast cancer is age. With advancing age there is a corresponding increase in breast cancer incidence.[6] The disease is rare in women under the age of 30. The largest number of cases appears within the 50-54 year group and this finding is associated with the detection of cases through routine breast screening of women aged 50-64 years.[51] It has been established that reproductive risk factors for breast cancer include; nulliparity, delayed first full term pregnancy, early menarche and late menopause.[52,53] It would appear that breast cancer risk is substantially determined by the number of ovulatory cycles a woman has in her lifetime and thus her exposure to ovarian estrogen. Women who experience early menarche or who experience a late menopause have an increased risk of developing breast cancer. Family history of breast cancer accounts for up to 10% of breast cancer in women in Western countries. Inherited faulty genes can also bestow a familial predisposition to breast cancer. Mutations of *BRCA 1* gene are associated with increased susceptibility to breast and ovarian cancer.[13]

Recent research from the Million Women Study [54] has demonstrated that current and recent use of hormone replacement therapy (HRT) is associated with an increased risk of incidence and fatal breast cancer. The Collaborative Group Study on Hormonal Factors in breast cancer [55] showed a small excess risk of breast cancer in current and recent combined contraceptive pill users. A strong relationship exists between weight and breast cancer risk; being overweight after the menopause increases the risk of breast cancer.[56-58] Recent evidence has shown that being overweight at point of diagnosis is related to poorer survival.[59,60] This effect is thought to be due to the conversion of adrenal androgen to oestrogen in adipose tissue, thus increasing the level of circulating oestrogen in the body.[61] A review of case-control studies suggests that alcohol consumption is associated with a modestly increased risk of breast cancer in women with non-proliferative breast disease.[62] Neither smoking or dietary fat intake have been shown not to have a particularly strong or consistent relation to breast cancer.[53] Systematic review evidence has demonstrated that an inverse relationship has been shown to exist between level of physical activity and risk of breast cancer of studies.[63,64]

1.6 BENEFITS OF EXERCISE IN OTHER CHRONIC CONDITIONS

The Chief Medical Officer's report titled "At Least Five a Week" [65] highlighted the role that physical activity can offer, both as a preventative measure and rehabilitation management strategy, in several medical conditions including arthritis, pulmonary disease, coronary heart disease, stroke, hypertension, renal disease, non-insulin dependent diabetes and cancer. Strong evidence on the positive impact of physical activity exists for several medical conditions such as coronary heart disease, [66] non-insulin dependent diabetes , stroke, hypertension, musco-skeletal disorders and metal health problems, [67] thus posing the question of whether exercise may also be a

therapeutic intervention in cancer patients. It is recommended that to gain the potential health benefits of physical activity individuals should aim to engage in thirty minutes of moderate intensity physical activity on at least five days of the week. Furthermore, participation should be regular-and sustained.[65]

1.7 CURRENT CANCER REHABILITATION PROVISION IN THE U.K.

To date, most QoL interventions that aim to address the needs of breast cancer patients have focused upon psychosocial therapies such as cognitive-behavioural counselling, information and education strategies, psychotherapy and social support.[68] However, these types of interventions are deemed to demonstrate modest efficacy and do not address the physical and functional concerns that breast cancer patients may experience such as fatigue, weight gain and reduced functional capacity. Although physical fitness would appear to be an important attribute of health, the role and value of exercise therapy as an aid to promoting adjustment in cancer patients has not yet been fully researched and explored in the UK. As such, the use of exercise as a therapeutic intervention within cancer care in the UK is rare [69] and warrants further research and evaluation.

1.8 THE RATIONALE FOR EXERCISE IN CANCER REHABILITATION

It has been reported that for some time after treatment has finished, breast cancer patients have persistent physical, emotional and social needs that contribute toward and impact upon overall QoL and satisfaction with life.[70-72] Fatigue, difficulty sleeping, pain and the psychological burden related to the uncertainty and fear of disease recurrence accompany the post-treatment period for some women.[73-75] Courneya and Friedenreich have reported that breast cancer patients perceived physical function to be the most important element affecting satisfaction with life, however it was also the

element that was least possessed.[76] The necessity and importance of measuring selected QoL outcomes in oncology is summarised by Montazeri who suggested that "adding life to years" as well as attempting to "add years to life" is an important task in cancer rehabilitation.[77] Thus, cancer care interventions should be directed toward QoL issues as well as promoting longevity. Maximising the physical and psychological functions that are affected by the disease and treatment are pivotal to the restoration and further improvement in patient's QoL. Quality of life has been described as being made up of many component parts including physical, functional, emotional, cognitive, spiritual and social dimensions.[78] As such QoL is multi-dimensional, reflecting a number of life domains.[79] Each domain may be perceived differently and personally judged based upon the individuals own subjective criteria for that domain.[80] Due to the broad nature of QoL several measures have been utilised across studies to measure global and the multi-dimensional components of cancer-specific QoL.[79]

1.9 EXERCISE BEHAVIOUR AFTER BREAST CANCER DIAGNOSIS

Recent research in breast cancer patients has shown that in making the transition from treatment to recovery physical activity is a key concern, followed by stress and fatigue.[71] It has been suggested by Demark-Wahnefried that breast cancer patients may seek to initiate new health behaviours (such as uptake of physical exercise and implementing dietary changes), after their diagnosis and cancer treatment, to improve their long term-health.[81] This enthusiasm however, may be tempered by an uncertainty regarding how to initiate or resume exercise.[34]

Irwin and colleagues reported that breast cancer patients decreased their physical activity levels by 11% from pre-diagnosis to post diagnosis [82] and found that only 32% of breast cancer patients were meeting the recommended levels of physical activity

(150min/wk^{-1}).[83] This evidence highlights the challenge of helping women treated for breast cancer to initiate or resume physical activity. In addition, those women who underwent chemotherapy and radiotherapy treatments experienced greater reductions in their physical activity levels (by 50%) compared to women who underwent surgery only. Additionally, obese women experienced greater reductions (by 41%) in their physical activity levels compared to their normal weight counterparts (by 24%). These findings highlight the need for strategies to manage the consequences of inactivity that may occur as a result of cancer treatment, particularly adverse changes in weight gain and body composition, [84] which have been reported to negatively influence breast cancer prognosis.[59] Furthermore, there may be a need to attenuate the potential for and management of possible late effects of breast cancer treatment such as osteoporosis, cardiovascular and pulmonary toxicities and lymphoedema.[85,86]

CHAPTER 2. LITERATURE REVIEW

2.1 RELATIONSHIP BETWEEN EXERCISE AND QUALITY OF LIFE IN BREAST CANCER PATIENTS

Evidence from observational studies has demonstrated a positive association between self-reported exercise and measures of psychological and physical well-being in breast cancer patients. Exercise participation has been shown to result in improved physical functioning, [87] quality of life (QoL) [88], mood [89], self-esteem [73] and coping [89] in breast cancer patients. Blanchard et al [90] suggested that it may not be the specific quantity of physical activity that determines gains in QoL but rather the positive change in physical activity level of breast cancer patients. In their recent observational study Blanchard et al [90] found that patients of various cancer types, who maintained or increased their activity levels after diagnosis had a higher QoL compared to those who decreased their activity. Similarly, Kendall et al [91] found that among younger women, (40 years or younger at diagnosis) treated for breast cancer, those who increased their exercise level after diagnosis, had higher mental health scores than those who did not. Encouragingly, research by Rabin et al [92] has shown that QoL gains are within the grasp of sedentary breast cancer patients. Rabin reported that previously sedentary breast cancer patients could achieve similar benefits on selected behavioural and psychosocial variables as regularly active breast cancer patients after a 12 week physical activity intervention.[92] Furthermore, breast cancer patients may be able to improve their prognosis and observational evidence has shown that women treated for breast cancer who are able to meet the US recommended physical activity levels may improve their survival.[93]

2.2 A GROWING BODY OF EXERCISE RESEARCH EVIDENCE

Over the last decade the number of studies investigating the role of exercise as a rehabilitation intervention for breast cancer patients has grown. This is reflected in the number of descriptive commentaries, literature reviews [17,23,29,79,94-101] systematic reviews and meta-analyses [102-109] that have been published regarding the efficacy and effectiveness of exercise interventions with cancer patients both during and after treatment. In 2005 alone, five reviews in this field were published.[94,104,105,109] The systematic reviews published to date differ significantly in terms of the inclusion criteria used and the approach taken in assessing the methodological quality of included studies. Each of the reviews aims to summarise the evaluated evidence and draw conclusions as to the efficacy and benefit of exercise rehabilitation for cancer patients. An overview of recently published systematic reviews examining exercise intervention studies in cancer patients is shown in Table 2.1

Table 2.1 An overview of recent systematic reviews of exercise intervention studies for cancer patients

Author	Review	Authors conclusions
McNeely [102]	Meta-analysis of 14 randomised breast cancer trials during and post treatment, that examined either QoL, cardio-respiratory fitness of physical functioning as primary outcomes	Exercise is an effective intervention to improve QoL, cardio-respiratory fitness and physical functioning and fatigue in breast cancer patients.
Conn [106]	Meta-analysis of 30 studies during and post treatment. Minimum sample size of 5. Quasi- experimental and randomised controlled designs included.	Exercise interventions resulted in small positive effects on health and well-being outcomes in cancer patients.
Schmitz [105]	Systematic review of 32 controlled trials with meta-analysis, in cancer patients during and post treatment.	Physical activity improves cardio-respiratory fitness during and after cancer treatment, symptoms and physiologic effects during treatment and vigour post treatment.
Knols [104]	Systematic review of 34 controlled trials in cancer patients during and post treatment.	Cancer patients may benefit from exercise both during and after treatment. Specific beneficial effects may vary as function of stage of disease, nature of medical treatment and current lifestyle of the patient.
Oldervoll [108]	Systematic of 12 randomised controlled trials with cancer patients during and post treatment.	Cancer patients benefit from maintaining physical activity balanced with efficient rest periods. Complete knowledge about the type of exercise most beneficial for patients at different stages of disease progression is still lacking.

Author	Review	Authors conclusion
Markes [103]	Systematic Cochrane review of nine trials, randomised or non - randomised controlled trials with meta-analysis of exercise during adjuvant therapy for women with non-metastatic breast cancer	Exercise during adjuvant treatment for breast cancer can be regarded as a supportive self-care intervention which results in improved physical fitness and thus the capacity for performing activities of daily life, which may otherwise be impaired due to inactivity during treatment. Improvements in fatigue were ambiguous and there was a lack of evidence for improvement with exercise for other treatment-related side effects
Stevinson [107]	Systematic review of 33 controlled trials with meta-analysis, in cancer patients during and post treatment.	Exercise interventions for cancer patients can lead to moderate increases in physical function and are not associated with increased symptoms of fatigue. However, it is impossible from current evidence to determine whether exercise has long term beneficial effects on survival or QoL.
Galvao [109]	Systematic review of 26 experimental exercise intervention studies in cancer patients during and post treatment.	Evidence underlines the preliminary positive physiological and psychological benefits from exercise when undertaken during or after cancer treatment.

2.3 REVIEW OF EVIDENCE PROVIDED BY SYSTEMATIC REVIEWS

Of particular interest here are the studies undertaken post-cancer treatment, these post-treatment studies are evaluated together with during treatment studies in the published systematic reviews. The systematic reviews provided by Conn [106] and Galvao and Newton [109] aimed to synthesize research findings from all exercise interventions among mixed cancer populations and as such, this strategy reflects the broad scope of research practice currently taking place in the field by integrating pilot study work and studies of a non-controlled research design with small sample sizes (minimum five participants) along with larger randomised controlled trials (RCT). The clinical and methodological variance employed in aforementioned reviews limits their ability to provide conclusions as to the potential benefit of exercise rehabilitation for breast cancer patients.

The reviews provided by Stevinson, [107] Knols [104] Oldervoll [108] and Schmitz [105] however, only included trials of a prospective nature with controlled comparison arms drawn from mixed cancer populations. This was a pre-determined strategy to collate the best available evidence at the time (i.e. methodologically robust) from studies that the authors believed would provide the clearest indication of the effect of exercise interventions in cancer patients. Studies included participants who were cancer patients of any type or stage of cancer and who were at any point in their treatment or recovery. Oldervoll further restricted the inclusion criteria to studies that employed randomisation and excluded pilot studies and multi-component interventions where exercise was included with other therapies. The most recent systematic review and meta-analyses to be published is that by McNeely [102] exclusively examined the effect of exercise interventions in women with breast cancer. Only RCT's were included. Similar to the Stevinson review, [107] trials must have included a comparison group

either comparing the exercise intervention to placebo, standard care or controlled comparison during or post cancer treatment. Studies with additional treatment arms such as diet, were only included if the effects of the exercise could be isolated. Due to the narrow inclusion criteria only ten studies were identified in this review, of which four studies were conducted in patients who had completed their cancer treatment[110-113]

2.3.1 SYSTEMATIC REVIEW CONCLUSIONS AND LIMITATIONS

The evidence critically appraised by Stevinson [107] and McNeely [102] in their systematic reviews concluded somewhat cautiously that exercise is an effective intervention in terms of improving cardio-respiratory fitness and physical functioning, QoL and reducing symptoms of fatigue. Oldervoll [108] and Knols [104] similarly affirm that reviewed studies show some positive effects of physical exercise on fatigue, physical function and physical or muscular capacity both during and after treatment. According to McNeely's review [102], only three studies presented an acceptable level of data to assess QoL. Data from these studies were pooled inclusive of one post treatment study [113] and two during treatment studies [114,115] results showed that exercise was superior to controlled comparison in improving QoL. Oldervoll [108] found that three out of four studies reviewed found significant improvements in health-related QoL in the exercise group compared to the controls. Knols [104] also identified statistically significant results for QoL and psychological well-being outcomes after breast cancer treatment. In contrast, Stevinson [107] suggested that there were too many methodological weaknesses and inconsistencies between studies, hence there was not sufficient evidence to conclude that exercise has a direct effect on QoL and other psychological outcomes.

In summary, authors of systematic reviews and literature reviews, [94,102,104,107-109] conclude that in general exercise is likely to be beneficial for cancer patients, but also comment that specific benefits may vary as a result of the stage of disease, type of treatment received and current lifestyle of the patient.

2.4 EXPERIMENTAL EXERCISE INTERVENTION STUDIES POST BREAST CANCER TREATMENT

In addition, two RCT's [116,117] have been published recently which post-date previous systematic reviews and meta-analyses.[110-113,118-124] Prospective controlled clinical trials with appropriate comparison groups reduce the opportunity for research bias and confounding factors thus offering the best level of evidence from which to make inferences about an emerging clinical therapy. Studies of exercise interventions that are of a controlled experimental design exclusively with a breast cancer population conducted after cancer treatment are shown in Table 2.2

Table 2.2 Experimental post-treatment exercise intervention studies with breast cancer patients

Author Year Location	Design & methodological quality	Timing of intervention	Participants, Stage, Age	Intervention & control arms	Main Outcomes	Reported results	Authors conclusion
Nieman (113) United States	RCT R: yes B: not stated C: not stated I: no	Completed treatment within past 4 years. Post-diagnosis average 3yrs	16 women, stage I-III breast cancer Age range: 35-72yrs	1) Supervised weight training & 30 minutes aerobic walking program at 75% max HR, 3 days p/w for 8 wks 2) Control	6 minute walk test, heart rate, leg extension strength, change in natural killer cell activity	Exercise group significantly improved distance walked more than control group. No change in natural killer cell activity.	"moderate exercise over 8 wks has no significant effect on *in vitro* natural killer cells in breast cancer patients"
Segar (122) United States	Controlled cross over trial R: no B: no C: no I: no	Post-surgery mean 42 months (range 1-9months)	24 women Age range 30-65yrs	1) Unsupervised home based aerobic activity 2) Unsupervised home based aerobic plus behaviour modification All aerobic activity 4 days p/w for 10 weeks, 30 minutes per session at 60% HR max. 3) Control	Depression (BDI), anxiety, self-esteem.	Exercise groups combined for analysis. Depression decreased by 44% in exercise group and increased 13% in control group. Anxiety decreased by 25% in exercise group, and increased by 11% in control group. No change in self-esteem.	"mild to moderate aerobic exercise may be of therapeutic value with respect to depressive and anxiety symptoms but not to self-esteem"

Author Year Location	Design & methodological quality	Timing of intervention	Participants, Stage Age	Intervention & control arms	Main Outcomes	Reported results	Authors conclusion
Courneya [110] Fairey [125] [126] Canada	RCT R:yes B:yes C:yes I: no	Completed treatment. Post-treatment by 12 months	53 post menopausal patients stage I –IIIa. Age range 50-69yrs	1) Supervised aerobic cycle ergometer training 3 days p/w for 15weeks, 15-35min at 70-75% of VO_2max. 2) Control	QoL, peak oxygen consumption physical well-being, fatigue, body weight and BMI, skin-folds, happiness.	Exercisers significantly increased peak oxygen consumption and overall mean difference in QoL 8.8 points higher in exercise group relative to control. No change in body composition.	"beneficial effects on cardiopulmonary fitness, fatigue and some psychosocial outcomes post treatment"
Galantino [123] United States	Quasi-experimental R:yes B:not reported C:not reported I:no	Completed treatment in previous 12 months.	11 women stage II to IV. Age range 40-59yrs	1) Unsupervised home based Tai Chi classes & video, 3 days p/w for 6 weeks 2) Unsupervised home based walking & stretching 3 days p/w for 6 weeks.	Physical function, BMI, QoL (FACT-B), fatigue, skin-folds.	No significant differences between either group on any outcome. Trend toward reduced fatigue in both groups.	"Tai Chi may be beneficial in the management of cancer related fatigue as an adjunct to traditional exercise programs"

Author Year Location	Design & methodological quality	Timing of intervention	Participants, Stage Age	Intervention & control arms	Main Outcomes	Reported results	Authors conclusion
McKenzie (111) Canada	RCT R:yes B:not reported C:not reported I:yes	Completed treatment Post treatment 6.5 months	14 women stage I and II breast cancer with unilateral lymphoedema. Stage III lymphoedema and bilateral disease excluded Mean age 56yrs	Supervised 1) Progressive upper body strength and arm ergometry, 3 days p/w for 8 weeks 2) Control	QoL (SF36)	No changes in Lymphoedema. QoL increased in exercisers but not statistically significant.	"trend toward improvement in quality of life is an important reason to consider upper body aerobic exercise for secondary lymphoedema"
Pinto et al (124) United States	RCT R: yes B:not reported C:not reported I: no Statistically underpowered	Completed treatment. Diagnosed within previous 3 yrs.	24 women stage 0–II breast cancer. Mean age 53yrs.	Supervised 1) Aerobic exercise 3 days p/w for 12 wks at 60% - 70% HRR, hospital setting. (Encouraged to exercise once p/w at home) 2) Control	Graded exercise test, blood pressure, heart rate, POMS, Body esteem scale.	Exercise group improved significantly on physical condition & weight concern subscales of body esteem scale compared to control group at post test. No significant reduction in psychological distress for either group.	"there is a need for further studies examining distress, body image and fitness level changes in a larger sample with sufficient power to detect differences"

Author Year Location	Design & methodological quality	Timing of intervention	Participants, Stage Age	Intervention & control arms	Main Outcomes	Reported results	Authors conclusion
Mustian [112] United States	RCT R:yes B:unclear C: unclear I:no	Completed treatment. within previous 3 yrs.	31 women, stage 0-IIIb. Age range 33-78 yrs	1) 12 wks supervised Tai Chi Chuan (TCC) 2) Supervised psychosocial support (PST) educational/peer support/coping strategies. Both groups met 3 days p/w for 12 weeks. Each session lasted 60min.	HRQoL, fatigue, BMI, self-esteem scale	TCC group demonstrated significant improvements in HRQoL and trend toward improvement in self-esteem. PST group reported declines in both HRQoL and self-esteem at same time point.	"TCC may be effective in improving HRQoL and self-esteem among women diagnosed with breast cancer… but support therapy does not"
Schmitz [119] United States	RCT R:yes B:not stated C:not stated I: no	Completed treatment 4-36 months prior to baseline	85 women, stage I-III Age range 34-75yrs.	1) Twice weekly weight training for 12 months 2) Non-exercise parallel control 0-6 months then trained from 7-12 months.	Body weight, body fat	Significant increases in lean mass as well as significant decreases in body fat % between exercise & control group at 6 months	"twice weekly weight training is a safe exercise program ...that may result in increased lean mass as well as decreased body fat %"

Author Year Location	Design & methodological quality	Timing of intervention	Participants, Stage Age	Intervention & control arms	Main Outcomes	Reported results	Authors conclusion
Pinto [118] United States	RCT R: yes B: not stated C: not stated I: yes	Completed treatment. 2 yrs post diagnosis.	86 sedentary breast cancer patients Stage 0-II. Age range 32-75 yrs	1)12 weeks of home-based physical activity counselling delivered by telephone. Progression to 5 days p/w and 30 min by week 12. 2) Contact control	Physical activity recall, walk test, physical activity monitoring via accelerometer, stage of motivational readiness for physical activity, POMS, fatigue, Body esteem scale	Physical activity group reported significantly more minutes of physical activity higher energy expenditure p/w & increased fitness.	"intervention successfully increased physical activity, improved fitness"
Ohira [120] United States	RCT R: yes B: not stated C: not stated I: no	Completed treatment 4-36 months prior to baseline.	86 women Age range 34- 75yrs	1) Thrice weekly supervised weight training sessions for 3months followed by unsupervised weight training for next 3 months. 2) Control group	QoL) and depressive symptoms. Upper body & lower body strength.	Exercise group improved physical & global QoL - Improvement associated with changes in upper body strength. No change in depression.	"improved QoL, in part via changes in body composition and strength".

Author Year Location	Design & methodological quality	Timing of intervention	Participants, Stage Age	Intervention & control arms	Main Outcomes	Reported results	Authors conclusion
Matthews [116] United States	RCT R:yes B: no C:not reported I:yes	Completed treatment within previous 12 months.	34 women, aged 45 yrs and over, stage I or II breast cancer	1) 12 week home based walking program & telephone (15min) based exercise counselling calls. Aimed for walking on 5days p/w 30-40min (RPE 11-13). 2) Control	Physical activity, body weight, body composition.	94% intervention adherence. Significantly greater increase in walking for exercise in intervention group than usual care. No change in body composition or weight.	"safe and effective intervention for increasing short term physical activity levels in breast cancer patients"
Herrero [117] Spain	RCT R:yes B:yes C:yes I: yes	2-5 yrs post breast cancer treatment	16 post menopausal women, stage I - II. Age range 40-60yrs	1) Exercise intervention, 8 weeks x 3p/w 90min sessions aerobic and resistance training 2) Control	QoL cardio-respiratory fitness, strength endurance, functional muscle capacity, body composition	QoL, aerobic fitness, leg press & sit to stand test improved significantly in response to training.	"combined cardio-respiratory and resistance training, even of brief duration improves QOL & overall physical fitness"

Author Year Location	Design & methodological quality	Timing of intervention	Participants, Stage Age	Intervention & control arms	Main Outcomes	Reported results	Authors conclusion
Ahmed [121] United States	RCT R:yes B:yes C:yes I:no	Completed treatment in previous 4-36 months.	45 women Age range 34-75yrs	1)Twice weekly supervised weight training for 6 months 2) No exercise control	Lymphoedema Clinical diagnosis of lymphoedema or symptom changes.	None of the intervention group reported a change in arm circumference.	"Intervention did not increase the risk or exacerbate symptoms of lymphoedema, need to start re-evaluating common clinical guidelines that survivors should avoid upper body resistance activity"

Key RCT: Randomised controlled Trial. R: Randomisation procedures used. B: Blinding of assessors. C: Concealment of allocation. I: Intention to treat analysis. SD: Standard deviation. BMI: Body mass index. QoL: Quality of life. HRQoL: Health related quality of life. DEXA: Dual-energy X-ray absorptiometry, BDI: Beck depression Inventory, POMS: Profile of Mood States, HRR : Heart rate reserve, HR: Heart rate. RPE: Rating of perceived exertion.

2.4.1 EXERCISE INTERVENTION STUDIES WITH BREAST CANCER PATIENTS POST TREATMENT.

The majority of post-treatment RCT's with breast cancer patients have been conducted in the United States [112,113,118-124] and Canada [110,111,116,125-127] One post-treatment study investigating exercise and cardio-respiratory and QoL outcomes has recently been conducted in Spain.[117] To date no experimental studies focusing exclusively on a breast cancer population after cancer treatment have been completed in the United Kingdom.

2.4.2 EXERCISE MODALITIES EMPLOYED

The majority of trials involved aerobic type exercise interventions, such as walking and cycling. [110,118,122,124] A smaller number of trials have explored alternative types of exercise modality. Three recent trials employed interventions involving resistance exercise [119-121] and three trials explored a combination of aerobic and resistance exercise. [111,113,116,117] Mustian [112] and Galantino [123] investigated the less traditional exercise mode of Tai Chi.

2.4.3 SUPERVISED VERSUS UNSUPERVISED EXERCISE INTERVENTIONS

The majority of trials offered supervised individualised exercise prescription within a group setting, [110-113,116,117] one study offered supervised group aerobic training within the context of a hospital setting.[124] Another study initially offered a combination of supervised exercise training followed by a period of unsupervised training.[120] Studies that involved supervised exercise reported high attendance rates to the exercise intervention, ranging from 72% to 98.4%.[112,113,124,128] Other studies have taken a more pragmatic approach and have been conducted in the home setting.[116,118,119,122,123] Previous research studies have found that those patients who engaged in group exercise sessions gained beneficial psychosocial effects as a result of the social interaction between patients.[34,129]

2.4.4 DURATION OF EXERCISE INTERVENTIONS

The duration of exercise intervention varied throughout the trials. Most lasted for 6 to twelve weeks; [111,113,122,123] or for a slighter longer period of 12 to 15 weeks. [110,112,118,124] Only two trials initiated interventions that lasted six months [120,121] or longer. The longest intervention was that undertaken by Schmitz which asked patients to exercise for 12 months.[119]

2.4.5 QUALITY OF LIFE OUTCOMES

Of the thirteen post-treatment studies reviewed, six studies included QoL as an outcome. A 15 week supervised cycle intervention study by Courneya and colleagues [110] reported that the exercise group significantly increased their overall QoL as compared to the non-exercise control group. Furthermore the subscale of physical well-being and the breast cancer specific subscale also showed significant change differences between exercise and control group in favour of the exercisers. Differences between groups in changes from baseline to post-intervention were also observed for the outcomes of happiness, self-esteem and fatigue favouring the cycling exercise intervention group. The shorter duration six-week study by Galantino (2004) in contrast did not find any statistically significant differences between either Tai Chi, walking or control group. This may have been due to the small sample size (n=11) used in this study.

An upper body aerobic and strength exercise programme for breast cancer patients with lymphoedema [111] found no statistically significant improvement in QoL. This study also had a small sample size (n=14). However in contrast, a small pilot study by Herrero [117] did report significant improvements in both global and physical domains of QoL in response to an eight week combined aerobic and resistance training programme. Larger studies undertaken by Mustian (n=31) [112] and Ohira (n=86) [120]

found that exercisers significantly improved their health related QoL as compared to patients who underwent psychosocial support or control (no-exercise) comparisons.

2.4.6 PSYCHOLOGICAL WELL-BEING OUTCOMES

Positive psychosocial effects favouring exercisers relative to usual care have been observed including depression and anxiety, [122] self-esteem, [112] body esteem and mood [124] in breast cancer patients who have completed their treatment.

2.4.7 PHYSICAL FUNCTION OUTCOMES

The highlighted studies that have focused upon breast cancer patients after completion of treatment report significant improvements in walking distance, [113] cardio-respiratory fitness, [110,117] increases in lean mass and decreases in percentage body fat, [119] increased physical activity, [116,118] strength [117,120] and no adverse effects of exercise training on lymphoedema status.[111,121]

2.4.8 METHODOLOGICAL DIVERSITY OF STUDIES

To date, trials have displayed heterogeneity in many respects with regard to study design, age, type of treatment received, initiation of exercise intervention after cancer treatment and outcomes measured. Most of the experimental trials compared an exercise intervention with a usual care, no exercise comparison group, [110,111,113,117,118,122,124-126] or compared exercise to a no exercise comparison group which then trained later.[116,119-121] The study by Galantino [123] compared home based Tai Chi exercise with a home-based walking programme comparison group. Two studies compared an exercise intervention to psychological therapy/support interventions.[112,127]

Across all trials there were systematic differences across the timing of exercise intervention, this ranged from one week to 8.3 years after completion of cancer treatment, thus making comparisons between studies difficult and further making

inferences from such heterogeneous study findings problematic. In general, patients recruited into these studies were women with stage I to III breast cancer who had completed a variety of treatments including various types of surgery, and a combination of radiotherapy and/or chemotherapy. One study by Segar [122] restricted patient recruitment to women who had only completed surgical treatment and no other form of other adjuvant therapy.

2.4.9 LIMITATIONS OF STUDIES

Methodological limitations exist within some of the studies highlighted. Notably, some studies recruited small sample sizes with multiple study outcomes and assessment measures which creates difficulty in making inferences regarding the efficacy of exercise interventions.[95] There is a scarcity of long-term follow up data and lack of reporting of adverse events which has implications for assessing the benefits of exercise and its relative safety.

A main complication for interpreting the efficacy of exercise with breast cancer patients lies in the disparities that exist in defining "post-treatment".[102] Courneya and Friedenreich [130] have recently proposed the PEACE (Physical Exercise Across the Cancer Experience) framework which defines the cancer experience into six phases (pre-treatment, treatment, post-treatment and resumption) with associated outcomes (prevention, detection, buffering, coping, rehabilitation and palliation, heath promotion and survival) that may be influenced during each of the relative phases. This framework could help to direct future research investigations.

Furthermore, studies have not included appropriate exercise-placebo and comparison groups to rule out any attention effects [104] that may be present during supervised interventions. To date no RCT study with breast cancer patients has employed an exercise-placebo arm in their research design. Minimising the potential

for contamination in the comparison groups, adequate randomisation procedures, concealment of allocation, and blinding of outcome assessors should also be addressed appropriately to ensure the methodological rigour of trials.[95,108] Oldervoll [108] has suggested the need for greater clarity and transparency in reporting the exercise prescription/intervention, recruitment strategy and paying close attention to monitoring intervention adherence. Oldervoll [108] supports this request by suggesting that without detailed descriptions of recruitment and adherence data the results from studies may only be relative to an exclusive group of patients who are more motivated to take part in exercise rehabilitation programmes after their cancer diagnosis.

There have been recent recommendations to conduct more exercise trials to define the optimal timing, mode, frequency and duration of exercise prescription to gain empirical evidence about the psychological and physiological effects of exercise in breast cancer patients.[94,96,105] Pinto et al [29] has also called for prospective studies that address behaviour change after cancer diagnosis and treatment. It is likely that sedentary breast cancer patients will not only need intervention to help them adopt exercise but that they will also need additional support and tools to help them make successful and sustained behaviour change. Indeed an approach that aims to support exercise adoption and is based upon a theoretical model of behaviour change would seem fitting given that recent research by Carmack-Taylor et al [131] has shown that an intervention based upon cognitive-behavioural skills training alone, did not significantly promote routine physical activity in prostate cancer patients.

2.5 BEHAVIOUR CHANGE

A number of validated theoretical models have been proposed to facilitate understanding of exercise motivation and behaviour, these have inclued Ajzen's Theory of Planned Behaviour (TPB) ,[132] Bandura's Social Cognitive Theory (SCT), [133] and the Transtheoretical Model.[134] A brief explanation of each theory is given below,

accompanied by findings from exercise studies in breast cancer patients that have examined the determinants of exercise utilising the respective models.

2.5.1 SOCIAL COGNITIVE THEORY

Bandura's SCT [133] is based upon the principle of reciprocal determinism between the individual, the behaviour and the environment. Self-efficacy is considered a key organizing construct within SCT and reflects an individual's confidence in their ability to perform a certain behaviour. In a cross-sectional study of breast cancer patients during treatment, Rogers et al [135] found that higher daily energy expenditure was significantly associated with higher perceived task and barrier self-efficacy. Further positive influences upon energy expenditure included having an exercise partner and an exercise role model.

2.5.2 THEORY OF PLANNED BEHAVIOUR

The model that has been most often applied and examined in exercise behaviour change studies in breast cancer populations has been the theory of planned behaviour. Ajzen's TPB [132] proposes that a person's intention is the immediate determinant of a behaviour because it reflects a conscious decision to perform or not perform the behaviour. Intention is hypothesised to be determined by attitude, subjective norm and perceived behavioural control. Perceived behavioural control (PBC) is the perceived ease or difficulty of performing a behaviour and may directly predict the behaviour if it is an accurate reflection of the person's actual control over the behaviour. Attitude is a positive or negative evaluation of performing the behaviour that includes instrumental (i.e. useful/useless, harmful/beneficial) and affective (i.e. un-enjoyable/enjoyable, boring/fun) components. Subjective norm reflects the perceived social pressure that individuals feel to perform or not perform the behaviour. The summary proposition of the TPB is that individuals will be motivated to perform a behaviour when they evaluate it positively, believe it will be enjoyable, perceive that others approve and also perform

the behaviour, and believe that the behaviour is under their control and that they are capable of performing it. The theory of planned behaviour also proposes that attitude, subjective norm and PBC are determined by underlying beliefs.

To date there is limited information regarding the determinants of exercise after cancer diagnosis and treatment, with only three studies[136-138] exploring the variables within the TPB that may explain exercise motivation in breast cancer patients. All three studies reported that intention was a consistent independent predictor of exercise participation either during or post-treatment. Furthermore attitude, subjective norm, and perceived behavioural control were all responsible for explaining a proportion of the variance in intention. Table 2.3 presents a summary of studies that have utilised the TPB to examine the social cognitive determinants of exercise in breast cancer patients. All studies found support for TPB as a theoretical framework for understanding exercise behaviour in breast cancer patients.

Table 2.3 Studies examining the TPB determinants of exercise in breast cancer patients

Author	Sample	Research design and exercise intervention	Results
Theory of Planned Behaviour			
Courneya & Friedenreich [137]	164 patients during treatment	Retrospective	Intention & perceived behavioural control (PBC) were significant determinants of exercise during treatment. Attitude and subjective norm were significant determinants of intention.
Courneya et al [136]	24 patients post-treatment (current exercisers)	Prospective 12-week , twice weekly training programme for a dragon boat racing competition	Intention was a significant independent predictor of exercise adherence. Subjective norm was a significant determinant of intention.
Blanchard et al [138]	84 patients post-treatment	Cross-sectional	Intention was significant independent predictor of behaviour. Attitude and PBC were independent determinants of intention.

2.5.3 THE TRANSTHEORETICAL MODEL (TTM)

The Transtheoretical Model (TTM) presented by Prochaska and DiClemente [134] has also been proposed as a useful theoretical basis for understanding structured exercise behaviour. The TTM was developed as a framework to describe the different phases involved in the uptake and maintenance of a new behaviour. The original model was tested and refined within the context of behaviour change within smoking cessation.[134] However since its development it has been applied to other areas of health behaviour change such as structured exercise.[139] Drop-out from structured exercise has been reported as a major issue in health and clinical populations, however Dishman et al [140] suggested that appropriately tailored interventions can increase physical activity. Participants often need support beyond that of simple access to facilities, to fully understand why and how they can elicit health behaviour change. Thus the Transtheoretical model has gained widespread popularity and acceptance as a theoretical framework upon which to base counselling-based exercise interventions.[141] The TTM has four key elements, [142] 1) stages of change, 2) processes of change, 3) self-efficacy and 4) decisional balance. Each element is briefly described below.

The TTM proposes that individuals pass through a series of stages of change (SOC) when adopting a new behaviour.[134] The SOC represent ordered categories along a continuum of motivational readiness for change. These stages include "Pre-contemplation": during this stage individuals are not thinking about behaviour change or intending to take action to change behaviour patterns in the foreseeable future, usually measured as the next six months. "Contemplation": individuals are seriously considering behaviour change, intending to initiate behaviour change in the next six months. Individuals become more aware of the positive aspects associated with change

but are also very conscious of the negative aspects of change thus, creating ambivalence. "Preparation": the individual is intending to take action in the immediate future, usually measured as the next month and may be taking small steps towards changing their behaviour. "Action": the individual is actively undertaking changes to their health behaviour, such as making modifications to their lifestyle. "Maintenance": involves the individual sustaining change over a period of time and working to prevent relapse. A particular strength of the TTM is that it recognises that individuals differ in their readiness to engage in new behaviours and thus behaviour change is not a linear process but rather a dynamic one.[143] Implicit within the TTM are the "processes of change".

2.5.4 PROCESSES OF CHANGE

Movement between the stages of change are associated with a set of independent variables known as the processes of change, [134] which relate to "how" individuals change their behaviour. These processes are both cognitive and behavioural in nature. The first five processes are classified as experiential processes and include: consciousness raising, dramatic relief, environmental re-evaluation, social liberation and self re-evaluation. These experiential processes are adopted primarily in the early stages of behaviour adoption. The last five processes are labelled behavioural processes and are used in the later stages.[144] These include; stimulus control, helping relationships, counter conditioning, reinforcement management and self-liberation. Exercise interventions can be tailored around specific processes of change, thus more effectively supporting the needs of the individual at any given stage of their behaviour change. The processes of change as proposed by Prochaska and DiClemente [134] are summarised in Table 2.4

Table 2.4 Processes of change.

Process	Definition	
Consciousness Raising	Efforts by the individual to seek new information and to gain understanding and feed-back about the problem behaviour.	
Dramatic Relief	Experiencing and expressing feelings about the problem behaviour.	
Environmental Re-evaluation	Consideration and assessment of how the problem behaviour affects the physical and social environment.	**Experiential**
Social Liberation	Awareness, availability, and acceptance by the individual of alternative, problem-free lifestyles.	
Self-Re-evaluation	Emotional and cognitive reappraisal of values by the individual with respect to the problem behaviour.	
Stimulus Control	Control of situations and other causes, which trigger the problem behaviour.	
Helping Relationships	Trusting, accepting, and utilizing the support of caring others during attempts to change the problem behaviour.	
Counter-conditioning	Substitution of alternatives for the problem behaviour.	**Behavioural**
Reinforcement Management	Rewarding one-self or being rewarded by others for making changes.	
Self-Liberation	Choice and commitment to change the problem behaviour, including belief in the ability to change.	

Despite it's popularity and the TTM's tenet for tailoring interventions based upon stage membership and the subsequent use of the processes of change, [144] thus guiding researchers in the "how" and "when" to use specific change strategies, the TTM has recently received some criticism regarding its effectiveness as a basis for exercise interventions.[145-147] A possible weakness of the TTM is that exercise behaviour may be more complex than previously recognised, sometimes reflected in the incoherent movement between the proposed stages of change and the use of the processes of change may be different to that experienced during smoking cessation.[139,145] However the TTM has gained support as providing a useful insight and understanding of the complex processes involved in exercise behaviour change. A systematic review by Adams and White [147] which examined 16 interventions aimed at promoting physical activity levels concluded that interventions based upon the TTM were effective at promoting physical activity adoption. A recent meta-analysis that summarised the applications of the TTM to physical activity and exercise [148] reported that in general there is support for the use of the TTM as stage membership is associated with differing levels of physical activity, the use of process of change, self-efficacy and decisional balance and therefore the TTM offers researchers a practical guiding framework upon which to base interventions.

2.5.5 SELF-EFFICACY

The concept of self-efficacy is considered to underpin the different stages of the TTM, [134,144] thus the individual is able to act as their own agent for change. Examples of an individual's self-efficacy within an exercise context would include the ability to overcome common barriers to exercise participation such as lack of time, not wanting to exercise in bad weather and the need to travel to an exercise venue. Research has shown higher self-efficacy is reported by those individuals who are in the action and

maintenance stages than those in the earlier stages.[149,150] Therefore individuals may benefit from interventions that focus on enhancing efficacy expectations relative to their stage of current behaviour change.

2.5.6 DECISIONAL BALANCE

Decisional balance is a key element within the TTM and can be seen as a useful predictor of an individual's movement between the stages within the TTM.[144] It is based upon a comparison of the perceived positive and negative aspects of adopting or maintaining a behaviour. Research has shown that during the early stages of behaviour change the disadvantages of change or the "cons" outweigh the advantages or "pros" of change. In the later stages of action and maintenance this weighing up of advantages and disadvantages may be reversed.[151] This would suggest that influencing perceptions of pros and cons could assist in the transition through the stages of change.

2.6 THE PRESENT STUDY

Based upon the current limited evidence-base and the shortfalls in the previous research as highlighted by the systematic reviews, there appears to be a need to conduct additional methodologically robust RCT's [108] to determine the efficacy of exercise upon psychological well-being and physical function in breast cancer patients after cancer treatment. The majority of current evidence is drawn from North America [107] making it difficult to generalise across a range of cultural and socio-economic populations, therefore a UK-based study is timely. In order to rule out the possibility of an attention-placebo effect via supervised exercise interventions, it has been suggested that RCT's should be designed with appropriate comparison groups.[104,109] Therefore the present study will include exercise and usual care groups but it will also include an exercise-placebo (attention-control) group in an attempt to control for possible social interaction effects that could potentially influence QoL and psychological well-being in

breast cancer patients. This methodological addition would help to further determine the efficacy and role of exercise therapy in cancer rehabilitation in the UK. An exercise intervention that is conducted within a supervised, controlled environment would also allow the dose of exercise achieved by breast cancer patients to be objectively recorded. Previous studies conducted overseas with breast cancer patients [110,113,116,122] have demonstrated that 30 minutes of aerobic activity on three days per week could be safely tolerated by breast cancer patients who were post-treatment. The present study will test whether this dose of exercise is also feasible and beneficial in a UK-based population.

2.6.1 THESIS AIMS

The aim of the first study was to examine the efficacy of exercise therapy upon QoL life and psychological well-being in women who have been treated for breast cancer. This study was a pragmatic RCT that tested the hypothesis that an exercise therapy intervention would lead to significant improvements in participants' QoL, psychological well-being and physical function. Additionally, it was hypothesised that over time, exercise therapy participants would increase their exercise behaviour compared to exercise-placebo (attention-control) and usual care groups. The second study was a qualitative study that aimed to explore the exercise experiences of participants that had taken part in the study.

2.6.2 STUDY OBJECTIVES

(1) To determine the differences in health-related outcomes from baseline to eight weeks and 24 weeks follow-up in women assigned to exercise therapy, exercise-placebo (attention-control) or a usual care control group.

(2) To investigate the effectiveness of exercise therapy in changing exercise behaviour and attitudes in breast cancer survivors by including a 24 week follow-up assessment of outcomes measures.

(3) To provide an overview of the effectiveness of different strategies used to recruit participants into the study

(4) To provide descriptive data regarding the exercise adherence of women allocated to the exercise therapy intervention, inclusive of the duration, rating of perceived exertion (RPE) and heart rate (HR), over the course of the intervention.

(5) To gain an insight into the personal experiences of participants who had taken part in the exercise interventions by conducting a qualitative, interview-based investigation.

CHAPTER 3. METHODS

3.1 PARTICIPANTS

Women who had completed breast cancer treatment were invited to take part in this study. All participants continued to receive usual care from their oncology health care team. Participants were recruited on the basis of the following inclusion and exclusion criteria:

3.1.1 INCLUSION CRITERIA

I. Female aged 18-65 years.

II. Participants should have completed their breast cancer treatment (excluding hormonal therapy), (i.e. surgery, radiotherapy and chemotherapy) more than 12 months and less than 36 months prior to joining the study.

III. Participants on hormonal therapy such as Tamoxifen, Arimadex and other endocrine treatments were eligible to take part in the study.

IV. At entry to the study participants must have been an exercise pre-contemplator, contemplator or preparer as defined by the Transtheoretical Model (152).

In the context of this study exercise is defined as "planned, structured and repetitive bodily movement done to improve or maintain one or more components of physical fitness".[153]

3.1.2 EXCLUSION CRITERIA

I. Participants with metastatic breast cancer and inoperable or active loco-regional disease were ineligible to take part.

II. Participants who have any physical or psychiatric impairment that would compromise their physical mobility and thus make them unable to undertake the physical requirements of the study interventions. For example, participants who suffered from conditions such as severe nausea, anorexia, chronic fatigue syndrome, severe arthritis and multiple sclerosis were not eligible.

III. All participants must have been willing to accept randomisation to any arm of the trial.

IV. Participants must have been willing to attend supervised exercise sessions three times per week for eight weeks.

3.1.3 PATIENT RANDOMISATION

Participants were randomised to one of three groups: (i) supervised exercise therapy (ii) exercise-placebo (attention–control) or a (iii) a usual care group. Randomisation to the three arms was on a 1:1:1 ratio and was performed using stratified random permuted blocks (with block size 6). Participants were stratified by type of adjuvant therapy (previous chemotherapy versus no previous chemotherapy) and current use of hormone therapy (yes/no). A distant telephone randomisation service was employed to allocate participants to the groups. Randomisation took place after participants had completed their baseline assessment. Ethical approval for this study was gained from the South Sheffield Research Ethics Committee (application number 02/226).

3.1.4 RECRUITMENT OF PARTICIPANTS

Treating oncologists and surgeons from Weston Park Hospital, Sheffield generated patient lists of potentially eligible patients and these were screened to identify eligible patients. A letter of invitation and a brief trial outline sheet (see Appendix 1) was sent by the treating oncologist/surgeon. Chapter 6 gives a detailed account of participant recruitment into the trial, outlining the effectiveness of the recruitment strategies employed and the social and demographic characteristics of responders and non-responders to the various recruitment strategies.

Interested participants were asked to contact the trial research assistant to gain further information about the study and were then invited to the Centre for Sport and Exercise Science (CSES) at Sheffield Hallam University to attend a familiarisation session with the research assistant, this lasted approximately 45minutes. The familiarisation provided the opportunity to give an in-depth explanation of the study and answer participants queries, and further confirm participants eligibility in terms of their exercise status (stage of change for exercise) [154] (see Appendix 2) and provide participants with a patient information sheet (see Appendix 3) and a consent form (see Appendix 4). A Physical Activity Readiness Questionnaire (PAR-Q) (see Appendix 5) [155] was administered and responses recorded by the research assistant at the familiarisation meeting. An appointment was subsequently made for participants to return for their baseline assessment with their completed written consent from. Demographic data including age, ethnicity, number of children, marital, smoking, occupation and education status were recorded at this time. Additional clinical information regarding the stage of disease, presence of lymphoedema and months since treatment completion were requested from participants.

A standard letter was sent to participants' general practitioners (GP) informing

them of their patients' involvement, accompanied by a trial outline sheet. If required, participants with elevated blood pressure defined as >145 systolic and > 95 diastolic were referred to their GP for medical clearance to take part in the study. To facilitate recruitment and retention a £20 sport store voucher was given to participants at the end of the intervention phase after the study and a contribution of £2.50 towards travel expenses was made per visit to the trial centre.

3.1.5 SAMPLE SIZE CALCULATION

A formal power calculation was made based on The Functional Assessment of Cancer Therapy-General (FACT-G) QoL scale.[156] The minimally clinically important difference for the FACT-G has been established as five to six points.[157] A recent UK pilot study involving breast cancer patients undergoing a group-based exercise intervention reported a mean difference of 15 points from baseline to 12 weeks post–intervention on the FACT-G scale.[115] The current study aimed to recruit a substantially larger and more diverse socio-economic group of women than included in the pilot trial and therefore was powered to detect a smaller change of 10 points on the FACT-G scale between exercise and usual care groups at an alpha level of $p<0.05$. The study needed to recruit at least 38 participants in each group to provide 80% power ($p<0.05$). The primary outcome of interest in this study was the mean difference between groups in FACT-G scores at baseline and eight weeks post-intervention.

3.2 MEASURES AND INSTRUMENTS

3.2.1 QUALITY OF LIFE (QOL)

The Functional Assessment of Cancer Therapy-Breast (FACT-G) [156] scale gives an overall QoL score based upon four subscale scores, which encompass physical, functional, emotional and social/family well-being domains. The reliability, validity and sensitivity of the subscales of the FACT-G have been tested with large numbers of

cancer patients and oncology specialists.[156] Respondents are asked to denote their agreement to each item on the subscales utilising a five-point scale of agreement from "not at all" to "very much". An additional breast cancer specific concerns subscale was also utilised, when this subscale is added to the FACT-G, the FACT-B scale emerges which reflects specific breast cancer concerns. (see Appendix 6).

3.2.3 PHYSICAL SELF-PERCEPTIONS

Physical self-perceptions were assessed using the The Physical Self-Perception Profile (PSPP) developed by Fox and Corbin.[158] The profile measures a multidimensional overview of an individual's perceived self-esteem in the physical context. Thirty items are rated on a four point scale. There are five subscales each consisting of six items. Subscales are perceived sports competence, attractiveness of body (appearance), physical condition, physical strength and general physical self-worth. This scale has demonstrated validity, reliability and sensitivity across different populations including middle-aged females.[158-160] (see Appendix 7).

3.2.4 FATIGUE

Fatigue is a common and debilitating side effect of cancer treatment and has been shown to be correlated with physical and psychological symptoms both during and after cancer treatment.[37] The Revised Piper Fatigue Scale [161] is a 22 item, 10-point self-report scale that measures overall fatigue, as such it was adopted in this study to assess level of fatigue. The scale comprises four dimensions of fatigue: cognitive/mood (6 items), behavioural/severity (6 items), affective meaning (5 items), and sensory (5 items). Each question was scored on an 11-point numerical scale. An overall average score is obtained, ranging from 0-10. A score of 0 indicates no fatigue and 10 indicates the most severe fatigue. Scores of 0-3 represent no or mild fatigue levels, scores 4-6 represent moderate levels and scores 7-10 represent high levels of fatigue. A change of

one unit in the fatigue score represents a clinically important change.[161] The PFS has demonstrated validity and reliability in studies with cancer patients [162] including breast cancer patients.[19] (see Appendix 8).

3.2.5 SATISFACTION WITH LIFE

The Satisfaction with Life Scale (SWL) [163] enabled the respondent to make a judgement about her subjective well-being and thus overall satisfaction with life based upon her own evaluative criteria. Life domains such as health and family are not specifically assessed, rather the respondent uses her own set of unique criteria to evaluate her satisfaction with life. The scale contains only five items which are rated on a seven-point scale from "strongly disagree" to "strongly agree". Higher scores represent greater satisfaction with life. The scale has demonstrated it is a highly reliable and a valid measure of life satisfaction.[163,164] This scale has been used to measure satisfaction with life in breast cancer patients who were undergoing adjuvant breast cancer treatment [115] and in women who had completed treatment.[72] (see Appendix 9).

3.2.6 DEPRESSION

The Beck Depression Inventory-II (BDI-II) [165] is a 21-item self-report instrument for measuring the presence and degree of severity of depression in adults. The BDI–II consists of 21 inventory items, each of the 21 items of the BDI-II represents a symptom or attitude that are specific to depressed patients. Each item consists of a list of four statements arranged in ascending severity about a particular symptom of depression. The respondent selects one statement that most closely reflects how they were feeling in the last week. Higher scores indicate greater depression. Studies of the internal consistency stability of the instrument reflect the inventory's high degree of reliability.[165,166] The BDI has been used to measure depression in breast cancer patients who had undergone surgery.[122] (see Appendix 10).

3.2.7 THEORY OF PLANNED BEHAVIOUR VARIABLES

The Theory of Planned Behaviour (TPB) as proposed by Ajzen, has been identified as a useful framework for understanding exercise behaviour.[167,168] The theory suggests that an individuals' intention to exercise and future behaviour are a product of their attitude towards the behaviour, subjective norms, and perceived behavioural control.[132] In this study participants' attitudes towards exercise participation, subjective norm and perceived behavioural control and intention to exercise were recorded. Example statements include "Exercise is enjoyable", Most people who are important to me encourage me to participate in regular physical exercise," "If I wanted to, I could easily take part in regular physical exercise", "I am going to take part in physical exercise as much as I can every week". Blanchard and colleagues [138] Culos- Reed et al [169] and Courneya and Friedenreich [137,170] have reported that TPB is a useful model for understanding the determinants of exercise behaviours in breast cancer patients. (see Appendix 11, 12 & 13).

3.2.8 EXERCISE BEHAVIOUR

The stage of change ladder for exercise [154] was used to confirm participants exercise behaviour at various time points throughout out the course of the study. The visual analogue measure depicts rungs on a ladder with corresponding labels that represent the level of physical exercise that is needed to satisfy each of the exercise stages of change. The stages are defined as pre-contemplation, contemplation, preparation, action and maintenance stages and participants assign themselves to one of these categories.[149] Past exercise behaviour was assessed by asking participants to consider how often they have participated in one or more physical activities for 20 to 30 min per session during their free time in the last three months?" This simple method for assessing behaviour was based on previous validated studies and the test-retest

reliability of this scale has been reported to be 0.64.[171-173] (See Appendix 2 for a copy of the stage of exercise change ladder and past exercise behaviour question).

3.2.9 PHYSICAL OUTCOME MEASURES

After surgical intervention for breast cancer some women experience reduced range of motion in the shoulder joint, which may impact on daily activities such as dressing, washing and performing routine tasks. Additionally some women may be suffering from lymphoedema which may elicit similar functional limitations. Measurement of shoulder related disability was assessed using a validated 22-item shoulder disability questionnaire.[174] Participants were asked to respond on the basis of how they felt on the day they completed the questionnaire, rather than recalling previous experiences.

Physical outcome measures included assessment of blood pressure and resting heart-rate, height, weight, body mass index (BMI), body composition, cardio-respiratory fitness and muscle function. Physical measures were administered in the sequential order as described above. After a five minute seated rest period blood pressure (mm/Hg) and resting heart-rate (bpm) were measured using the OMRON® M5-I blood pressure monitor (OMRON® Hoofdorp, The Netheralands) in accordance with the American College of Sports Medicine (ACSM) (2006) [175] guidelines. The blood pressure cuff was placed on the contra-lateral arm, thus avoiding any exacerbation of lymphoedema. In the case of bilateral surgery the participant advised the side to be measured based upon the advice they had been given by their oncologist/breast care nurse. Height was measured with shoes removed, the participant was asked to stand upright hands by sides and head level, with eyes focussed ahead. Height was recorded to the nearest point one of a centimetre. With shoes removed and wearing the same type of clothing as on previous weighing, participants' were weighed using scales

(Seca, Germany), weight was measured in kilograms (Kg) to the nearest point one of a kg and also recorded in pounds of bodyweight (required data for body composition analysis).

Calculation of body fat percentage was performed using Bioelectrical Impedance Analysis (BIA) [176] with a BodyStat 1500 monitoring unit (BodyStat Ltd. Isle of Man, U.K.). BIA reflects the degree of resistance to flow of electrical current in the body and from this body fat percentage is estimated. Body fat is a poor conductor of electrical current. To ascertain accurate and reproducible results on repeat tests the participants were prepared and the test administered in accordance with the recommended Bodystat guidelines.[177] Body Mass Index (BMI) [175] was used to assess weight relative to height. Obesity related health problems increase beyond a BMI of 25, [175] BMI was calculated by the BodyStat monitoring unit after input of height and weight data.

Cardio-respiratory fitness is an important component of physical function [175], Courneya and Friedenreich [76] have reported that breast cancer patients perceive physical function to be the most important element underpinning satisfaction with life. [175] Estimation of maximal oxygen consumption was assessed by a single stage sub-maximal walking test developed by Ebbeling et al.[178] The test protocol involves the participant establishing a self-selected brisk walking pace between 2.0 and 4.5mph. A four minute warm-up at 0% gradient is performed at the chosen walking pace, with the aim of eliciting a heart-rate of between 50-70% of age predicted heart rate-reserve. A second four minute stage is performed at the same walking speed on a 5% gradient. Heart-rate and rating of perceived exertion (RPE), [179] were recorded every minute throughout the test. A two minute cool down at a reduced walking speed with 0 % gradient was conducted. This protocol generates distance walked, heart-rate at eight

minutes and walking speed. Using the equation developed by Ebbeling [178] which takes into consideration gender, heart-rate, speed and age it is possible to estimate relative $\dot{V}O_{2\,max}$ from the sub-maximal stage at 5% gradient. This test has the advantages of being a familiar habitual exercise modality, is time-efficient thereby reducing assessment burden, walking speed can be individualised and is therefore practical for assessing functional capacity in participants of varying ages and fitness levels. The test has been validated with large numbers of participants of varying ages and gender. This test has been used previously with cancer populations.[180] Heart-rate was measured using a short range radio telemetry monitor (Polar Sport Tester, Kempele, Finland).

The Biodex Isokinetic Dynamometer (Multi-Joint Sytem 3, Biomedical Systems Inc, New York) was used to conduct a maximal 20 second isokinetic strength test involving knee extension/flexion of the quadriceps and hamstring muscles of both legs. Selected indices of muscle function included peak torque, torque relative to bodyweight and total work for the quadriceps and hamstrings.

Socio-demographic information was based upon The Index of Multiple Deprivation (IMD) [181] rank score, which was calculated for each participant based on their residential postcode. This measure of deprivation encompasses seven domains, income, employment, health and disability, education, skills and training, barriers to housing and services, living environment and crime.

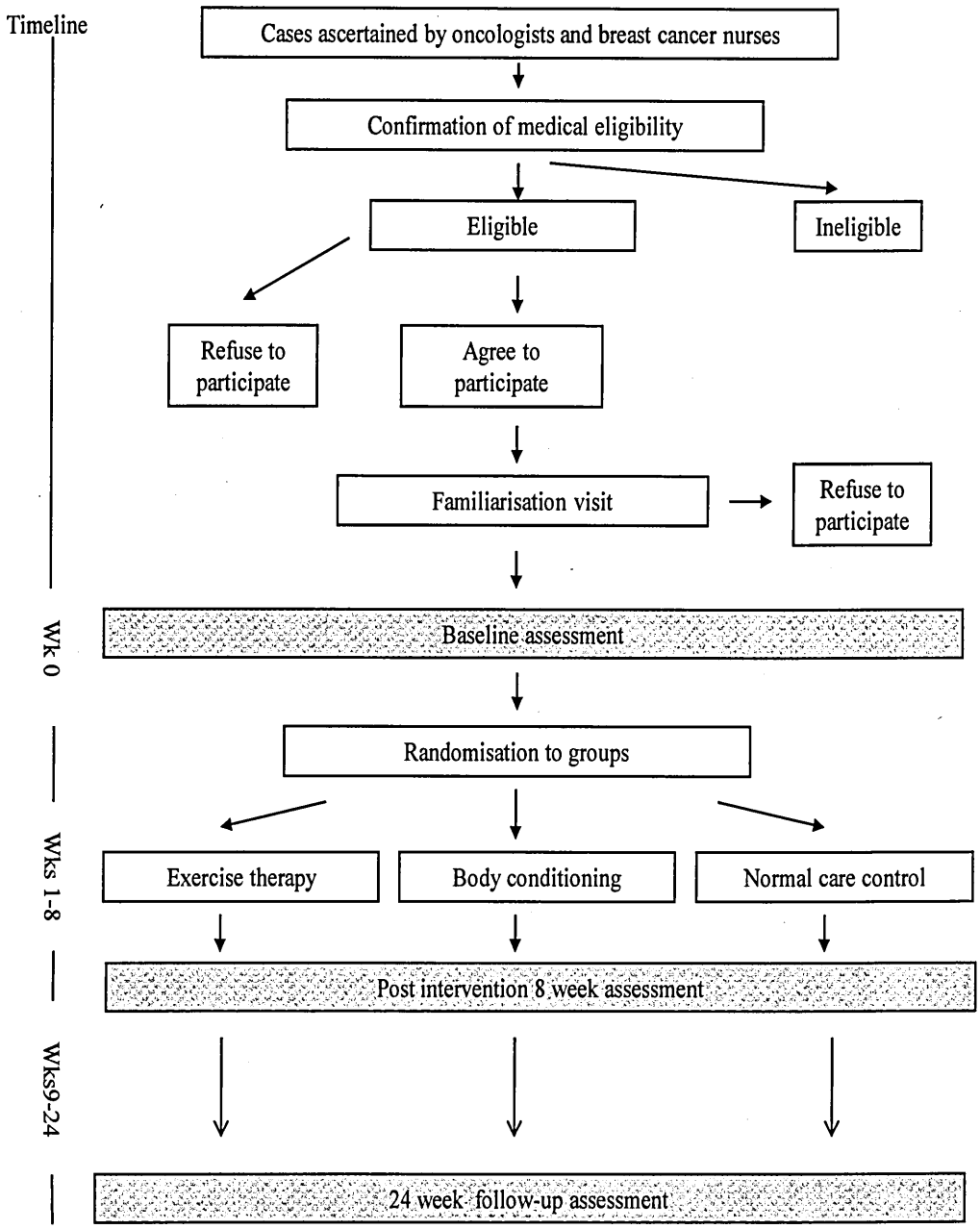
All physical assessments and questionnaires were completed within one week of completing the final exercise session or in the case of the usual care group within one week of their assessment point. All baseline questionnaires were completed at the study centre. Participants were allowed to take questionnaires home to complete if this was deemed more convenient, and post back to the study centre in a stamped addressed envelope.

Completion of assessments took approximately one and a half hours to two hours. This level of burden was tolerated well by participants, however it would not be recommended to extend the assessment period beyond this time frame.

3.3 DESIGN AND ASSESSMENTS

The study was an intention to treat three (group) by three (time) RCT. All eligible patients, regardless of their compliance with the protocol were included in the data analysis. Outcome measures were completed at baseline, at the end of the eight-week intervention and at 24 week follow-up (Refer to Figure 3.1 for a schematic overview of the study design)

Figure 3.1 Overview of study



3.4 EXERCISE THERAPY INTERVENTION

The exercise therapy sessions took place at the Centre for Sport and Exercise (CSES) at Sheffield Hallam University. A dedicated exercise room, containing a variety of aerobic exercise equipment and floor space for stretching was used to for all sessions. All exercise therapy sessions were on a 'one-to-one' basis with the research assistant who was also trained as an exercise instructor who led the exercise sessions in this study. Each session lasted approximately 50 minutes and comprised of 30 minutes of moderate intensity exercise, with a warm-up and cool-down and 20 minutes of exercise counselling. Participants were offered a range of exercise modalities to choose from including, treadmill walking, stationary cycling, rowing and an elliptical cross-trainer (see Appendix 14). Participants were encouraged to choose their preferred exercise mode.

Exercise and cancer prescription guidelines advocated by Courneya [24] recommend cancer patients engage in 20-30 minutes of continuous exercise on at least three to five days per week. The exercise therapy sessions were developed with these guidelines in mind. Heart-rate (HR) was recorded every two minutes, participants wore HR monitors that relayed their exercising HR to a wrist watch display, allowing participants to easily monitor their exercise intensity. Training HR intensity was based upon 65%-85% of HR age adjusted maximum. Rating of perceived exertion (RPE) [179] was also recorded at the same two minute interval. To offer a pragmatic approach and maximise compliance to the exercise intervention, participants were offered sessions on various days and times. These included evenings and weekends. To minimise fatigue and promote adequate recovery, participants were advised to allow 24 hours between exercise therapy sessions. Refer to Table 3.1 for a description of the exercise intervention.

Table 3.1 Exercise therapy intervention

Exercise	Weeks 1-2	Weeks 3-4	Weeks 5-6	Weeks 7-8
Duration	10 min - 20 min,	15 min - 20 min	15 min - 20 min	20 -30 min
Type	Aerobic exercise (e.g. treadmill walking, cycling, rowing)	Aerobic exercise	Aerobic exercise	Aerobic exercise
Intensity (age-adjusted HR max.)	60% - 75%	60% - 75%	75% - 85%	75% - 85%
Frequency	3 times per week	3 times per week	3 times per week	3 times per week

Notes: Exercise sessions commenced and concluded with a 5 min warm up and cool down period. Women were encouraged to participate in continuous, rather than intermittent exercise bouts.

3.4.1 EXERCISE COUNSELLING

This study included exercise counselling as an integral component of the exercise therapy intervention. The Transtheoretical Model (TTM) presented by Prochaska and DiClemente [134] was developed as a framework to describe the different phases involved in the uptake and maintenance of a behaviour such as exercise. The TTM was used in this study to facilitate the exercise counselling process. Practical strategies and techniques for promoting behaviour change are supported by the "processes of change".[134] These processes are both cognitive and behavioural in nature. In accordance with the processes of change from the TTM, during the exercise counselling the research assistant facilitated a variety of cognitive-behavioural techniques for promoting positive exercise attitudes and experiences. Weeks one to four focused upon cognitively-based intervention strategies (e.g. consciousness raising and decisional balance appraisal). During weeks five to eight, more behaviourally-based interventions were introduced (e.g. goal setting, self-monitoring and finding social support), these sessions offered participants the opportunity to put into practice the new skills and behaviours participants had learnt in the previous weeks. Refer to Table 3.2 for a description of the exercise counselling topics.

At the end of the eight-week intervention the exercise therapy participants were encouraged to consider maintaining an exercise regime through a personalised plan that was tailored to suit their individual needs.

Table 3.2 Exercise Counselling Protocol

Weeks	Process of change	Exercise counselling framework: Examples of skills and techniques used
1-2 Cognitive	Consciousness Raising Dramatic Relief Decisional Balance	a. Principles of exercise. Information about the importance of warming up and cooling down Exercising safely What to wear, what & when to drink b. Fitting exercise into your life Finding time to exercise Try an activity log for a day/weekend day What to expect in the next few weeks c. Benefits of exercise Is it worth it? Weighing up the pros & cons Your expectations, hopes & wishes Contra-indicated exercises Exercising with lymphoedema
3-4 Cognitive	Self Re-evaluation Decisional Balance Consciousness Raising	d. Your exercise preferences Previous exercise experiences, why this worked/failed? What other exercises might you like to try? My priorities e. Do you know? How hard and how often should you exercise? Monitoring heart rate and perceived exertion Exercising for health or sport? How exercise fits into weight management f. How are you finding the sessions? What do you like/dislike? What would you change? Is it what you had expected? Feeling confident about exercise?

5-6 Cognitive and Behavioural	Self Re-evaluation Goal setting/self-regulation Social support	h. Active and healthy living Food groups, portion sizes. Hand out food diary (3 days). Understanding food labelling Try a Pedometer for a week - just how active are you? i. Introducing goal setting What is it? SMART principles How might it help? Exercise & healthy eating goals j. Finding support for exercise Thinking of others who might encourage participation in exercise What do friends & family think about exercise?
7-8 Behavioural	Goal setting/self-regulation Stimulus control Reinforcement Management Self -Liberation	k. Review food diary Making healthy food choices Keeping on track–rewarding myself m.Looking and planning ahead Thinking about moving on from the programme Future exercise options Why keep exercising? What will help me to exercise in the future? What will stop me? Possible pitfalls o. What have I achieved so far What do I want to achieve from here? What has been learned?

3.4.2 EXERCISE-PLACEBO (ATTENTION–CONTROL) INTERVENTION

An exercise-placebo (attention-control) group was included in this study in an attempt to control the potential for attention effects that might be associated with the exercise intervention. In order to offer a relevant and meaningful attention control group an alternative form of exercise was provided. Similar to the exercise therapy the exercise-placebo sessions offered were on a one-to-one basis with the exercise instructor. Participants assigned to the exercise-placebo group also attended the Centre three times per week for eight weeks, participating in 50 minute sessions. The exercise-placebo group participated in light flexibility, range of motion and body conditioning activities using a range of exercises tailored to participant's ability. Examples of exercises completed include flexibility, balance, mobility and general muscular conditioning (see Appendix 15). The physical exertion of each exercise was designed to be kept to a minimum but nevertheless activities were engaging and progressive in nature. It was necessary to equate social contact between the exercise groups and provide a meaningful alternative to exercise therapy that would hopefully facilitate compliance. Heart-rate and RPE were assessed every five minutes during the exercise sessions. The exercise-placebo group did not receive exercise counselling, instead, conversations were focused upon everyday topics such as families, news and weather.

3.4.3 USUAL CARE GROUP

The usual care group were encouraged to continue with their sedentary lifestyle as usual, they were asked not to engage in a structured exercise programme over the course of the eight-week intervention period. To reduce attrition the usual care group participants were offered the opportunity to attend up to six personalised exercise sessions with the research assistant after the 24 week follow-up assessment.

3.5 DATA ANALYSIS

Data were analysed on an intention-to-treat (ITT) basis, all eligible patients, regardless

of their compliance with the protocol were included in the analysis. Repeated measures mixed analysis was used to compare the majority of trial outcomes between the groups at eight and 24 weeks follow-up. An ANCOVA was conducted to allow for the adjustment of dependent variable mean values to account for the influence of one or more of the baseline covariates (such as age, treatment type and length, marital status) that are not controlled for by the research design. Given that cancer treatment is a lengthy and invasive process there was potential for these variables to influence exercise tolerance and response to exercise intervention hence this type of analysis was justified. The present study was a time (3) x condition (3) and as such an ANCOVA allows comparison of means of three or more groups. Treatment alone and in combination with time were considered as fixed effects, with baseline measurement as a covariate, time (eight weeks and 24 weeks follow-up) 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 stage of change (SOC) data were analysed with chi-squared tests (with Bonferroni corrections) by comparing the proportion of cases changing physical activity categories to become active at least three times per week and reaching the action or maintenance stage of change (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 1000 replicates was carried out to assess the reliability of results. This procedure showed that the p values from the mixed-model analysis were constant and therefore statistical inferences could be confirmed. Little's D test was used to examine whether missing data were missing completely at random. Method of data imputation was as directed by the FACT-G scoring guidelines. Analyses for physical activity level were performed comparing the proportion of patients that reported a change from being inactive at baseline (i e. never, once per month, 2 to 3 times a 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 eight-week follow-up because this measure assesses behaviour change over a period of six months. Analyses were performed comparing the proportion of patients that reported a change from being sedentary (i.e. pre-contemplation, contemplation and preparation) at baseline to being in the action or maintenance stages of change at follow-up between the groups.

CHAPTER 4.0 RESULTS

4.1 RECRUITMENT CHARACTERISTICS

Recruitment of participants took place between January 2003 and July 2005. The trial recruitment rate of eligible patients on the basis of recruitment via clinician letter was estimated to be 28.6%. From 572 initial enquiries, 108 patients were eligible, gave their consent to enter the study and were randomised to exercise therapy (n=34), exercise-placebo (n=36) or usual care (n=38). Chapter 6 provides more detailed information on the recruitment of participants into this study.[182]

4.2 DEMOGRAPHICS

The mean age of the sample was 51 years (SD±8.6) with an age range of 32-65years. The mean number of months post-breast cancer treatment (excluding hormonal therapy) was 17.4 (SD±6.7) with the mean length of treatment lasting 8 months (SD±5.1). The sample consisted of women who were predominantly of white ethnicity 98.1% and who had a mean percentage body fat of 40.3% (which is considered above the norm.[175] Similarly, mean body mass index (BMI) was 28.5 (SD±4.56) this corresponds to being overweight.[175] The average body weight of the sample was 76.1 kgs (SD±12.7). The mean value for aerobic fitness was 29.4 (SD±5.0), this equates to just above average for women aged 50-59years and below average for women aged 40-49years.[175] The majority of the participants were either married or co-habiting (89.1%). Most were non-smokers 90.7% and 83.3% were in employment. Breast cancer related lymphoedema was prevalent in 41.7% of the sample. Refer to Table 4.1 for baseline health behaviours, treatment and socio-economic characteristics of the sample by group allocation.

Table 4.1 Baseline socio-demographic, health behaviour and treatment characteristics

	Exercise therapy (N=34) Mean (SD) or N (%)	**Exercise-placebo** (N=36) Mean (SD) or N (%)	**Usual care** (N=38) Mean (SD) or N (%)
Age (years)	51.6 (8.8)	50.6 (8.7)	51.1 (8.6)
Smokers	0/34 (0)	5/36 (13.9)	4/37 (10.9)
Ethnicity			
White	34/34 (100)	35/36 (97.2)	37/38 (97.4)
Index of multiple deprivation (N=107)			
Quartile 1 (least deprived)	9/33 (27.3)	11/36 (30.6)	5/38 (13.2)
Quartile 2	10/33 (30.3)	9/36(25.0)	12/38 (31.6)
Quartile 3	6/33 (18.2)	11/36 (30.6)	12/38 (31.6)
Quartile 4 (most deprived)	8/33 (24.2)	5/36 (13.9)	9/38 (23.7)
Stage of change for exercise (SOC)			
Precontemplation/Contemplation	16/34 (47.1)	18/36 (50.0)	24/36 (63.2)
Preparation	18/34 (52.9)	18/36 (50.0)	14/36 (36.8)
Previous physical Activity			
Never	9/34 (26.5)	9/36 (25.9)	12/38 (31.6)
≤3 times per month	7/34 (20.6)	12/36 (33.3)	12/38 (31.6)
Once per week	11/34 (32.4)	9/36 (25.0)	9/38 (23.7)
≥Twice per week	7/34 (20.6)	6/36 (16.7)	5/38 (13.2)
Employment status			
Employed	26/34 (76.5)	25/36 (69.4)	21/34 (58.3)
Education			
Secondary & A levels	17/34 (50.0)	12/35 (34.3)	18/33 (54.5)
Degree	5/34 (14.7)	13/35 (37.1)	6/33 (15.2)
Other	12/34 (35.3)	10/35 (28.5)	9/33 (27.2)
Marital status			
Married/cohabitating	28/34 (82.4)	31/34 (86.1)	31/33 (81.6)
Single/widowed/divorced	6/34 (17.6)	5/34 (13.9)	7/33 (18.4)
Experiencing lymphoedema	16/34 (47.0)	11/36 (30.6)	18/38 (47.3)
Children	29/33 (87.9)	31/35 (88.6)	30/34 (88.2)
Months post treatment	17.6 (7.4)	18.2 (6.9)	16.7 (5.9)

Using hormone therapy	25/34 (73.5)	25/36 (69.4)	29/38 (76.3)
Treated with chemotherapy	27/34 (79.4)	25/36 (69.4)	28/38 (73.7)
Treated with radiotherapy	27/34 (79.4)	28/36 (77.8)	30/38 (78.9)
Treated with surgery			
Mastectomy	18/34 (52.9)	18/36 (50.0)	21/38 (55.3)
Breast conserving surgery	16/34 (47.1)	18/36 (50.0)	17/38 (44.7)

Note: SD= Standard deviation

4.3 BASELINE HEALTH BEHAVIOURS, TREATMENT, SOCIO-DEMOGRAPHIC CHARACTERISTICS OF THE SAMPLE

At baseline, information regarding participants' medical history relative to breast cancer diagnosis, health behaviours and socio-demographic characteristics were recorded. In general, the three groups were balanced at baseline in relation to demographic, breast cancer treatment and health behaviour characteristics. The groups were comparable at baseline with respect to socio-demographic, treatment characteristics, health behaviour and psychological health outcome variables. Table 4.2 displays the baseline data for QoL of life and psychological health outcomes by group. Table 4.3 displays the baseline data for physical health outcomes. There were no significant differences between the groups on their baseline physical activity levels.

Table 4.2 Baseline data for quality of life and psychological health outcomes

Outcome	Group					
	Exercise		Exercise-placebo		Usual care	
	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 (PWB)	23.65	2.97	22.92	3.88	22.21	4.98
Social/family well-being (SWB)	20.98	5.45	22.49	5.74	20.71	4.74
Emotional well-being (EWB)	17.12	4.25	17.58	4.57	18.32	3.65
Functional well-being (FWB)	18.66	6.26	20.58	4.85	19.28	6.00
Breast cancer subscale (BCS)	21.30	5.91	22.45	5.89	20.88	5.49
Satisfaction with life (SWL)	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
Intentions	5.12	1.23	5.85	1.22	5.49	1.06
No. of times intentions	2.78	0.83	2.72	0.74	2.63	1.00
Subjective norm	5.35	1.06	5.79	1.26	5.35	1.27
Perceived behavioural control (PBC)	4.76	0.94	5.03	1.20	4.77	1.04
Attitude	2.35	0.51	2.33	0.62	2.45	0.47

Note: SD=Standard deviation

Table 4.3 Baseline data for physical health outcomes

Outcome	Group					
	Exercise		Exercise-placebo		Usual care	
	Mean	SD	Mean	SD	Mean	SD
Weight (kg)	77.2	12.1	73.9	11.3	77.2	14.1
Body mass index (BMI)	28.5	4.4	27.6	4.1	29.6	5.1
%Body Fat	40.2	5.4	39.5	6.2	41.3	6.1
Aerobic fitness (ml/kg/min)	29.1	4.8	30.3	5.0	30.0	5.4
Systolic blood pressure	131	18	127	21	128	16
Diastolic blood pressure	87	12	86	11	86	9
Resting pulse	74	13	72	13	74	12
Shoulder	2.4	3.3	2.6	3.3	3.7	4.7
Quadriceps peak torque	79	14	78	16	78	22
Quadriceps peak torque/bodyweight	108.0	20	110	24	101	24
Quadriceps total work	1598	294	1583	405	1591	537
Hamstring peak torque	37	7	36	7	35	9
Hamstrings peak torque/bodyweight	50	11	48	11	46	12
Hamstrings total work	740	213	676	204	672	243

Note: SD=Standard deviation

4.4 QUALITY OF LIFE (QOL) OUTCOMES

Analyses identified a significant difference in QoL (primary outcome) on the FACT-G scores between exercise therapy and usual care groups at eight week follow-up, favouring exercise therapy (p=0.004; mean difference 9.8 units). This effect did not persist at 24 week follow-up. A non-significant mean difference of 6.62 units (p=0.117) was observed between exercise-placebo and usual care. The breast cancer specific FACT-B scale displayed a significant effect between exercise therapy and usual care (p=0.002) at eight week follow-up, favouring exercise therapy. A significant (marginal) effect was also seen at eight weeks in favour of exercise-placebo relative to usual care (p=0.049) although this effect was of a smaller magnitude than that observed for exercise therapy. With respect to the subscales of the FACT-G, significant differences were observed between exercise therapy and usual care at eight weeks for social well-being (SWB) (p=0.032), functional well-being (FWB) (p=0.014) and the breast cancer specific subscale (BCS) (p=0.038). Significant effects for the variables mentioned were always in favour of the exercise therapy participants. These significant differences were not present at 24 week follow-up. See Table 4.4 for the effects of exercise therapy and exercise–placebo relative to usual care on quality of life outcomes with means adjusted for baseline scores.

Table 4.4 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 diff, 95% CI)				24 (mean diff, 95% CI)			
		Mean	lower	upper	Adj P[1]	mean	lower	upper	Adj P[1]
FACT-G	Exercise therapy versus usual care	**9.80**	2.20	17.40	**0.004**	7.27	-0.51	15.06	0.081
	Exercise-placebo versus usual care	6.62	-0.90	14.15	0.117	4.72	-2.90	12.34	0.469
FACT-B	Exercise therapy versus usual care	**13.14**	3.44	22.84	**0.002**	8.14	-1.81	18.08	0.174
	Exercise-placebo versus usual care	**9.57**	0.04	19.10	**0.049**	5.89	-3.80	15.58	0.491
Physical well-being (PWB)	Exercise therapy versus usual care	1.69	-0.55	3.94	0.250	1.09	-1.22	3.39	0.746
	Exercise-placebo versus usual care	1.13	-1.07	3.33	0.667	0.67	-1.59	2.92	0.955
Social/family well-being (SWB)	Exercise therapy versus usual care	**2.58**	0.14	5.02	**0.032**	1.83	-0.67	4.33	0.279
	Exercise-placebo versus usual care	2.06	-0.35	4.48	0.140	0.81	-1.65	3.26	0.931
Emotional well-being (EWB)	Exercise therapy versus usual care	1.40	-0.95	3.74	0.513	1.62	-0.79	4.02	0.376
	Exercise-placebo versus usual care	1.48	-0.82	3.79	0.426	1.31	-1.04	3.65	0.585
Functional well-being (FWB)	Exercise therapy versus usual care	**3.71**	0.50	6.92	**0.014**	2.45	-0.84	5.73	0.263
	Exercise-placebo versus usual care	1.58	-1.57	4.73	0.689	1.85	-1.36	5.06	0.549
Breast cancer subscale (BCS)	Exercise therapy versus usual care	**3.37**	0.12	6.61	**0.038**	1.60	-1.72	4.91	0.727
	Exercise-placebo versus usual care	3.06	-0.11	6.24	0.065	1.79	-1.46	5.03	0.599

[1] Paired comparisons between groups at each time point were adjusted by the Tukey-Kramer method. Bold font indicates variables where significant difference exists between the groups and p values

4.5 DEPRESSION

There were significant differences in mean depression scores between exercise therapy and usual care (p=0.001) and also between exercise-placebo and usual care (p=0.001) at eight week follow-up. Exercise therapy participants reported slightly better depression scores than exercise-placebo participants at eight week follow-up. Usual care reported higher depression scores at eight weeks follow-up. The significant differences between the exercise intervention groups relative to usual care were evident at 24 week follow-up however, the magnitude of effect was smaller than that observed at eight week follow-up. Refer to Table 4.5 for the effects of exercise-therapy and exercise-placebo relative to usual care on psychological health outcomes.

4.6 FATIGUE

With respect to total fatigue, there was a significant difference between exercise-placebo and usual care at eight week follow-up, with the exercise-placebo participants reporting less fatigue compared to their usual care counterparts (p=0.037). Exercise therapy participants also recorded a non-significant trend toward less fatigue than usual care participants (Refer to Table 4.5).

4.7 SATISFACTION WITH LIFE

A significant difference in mean in Satisfaction With Life (SWL) scores between exercise-placebo and usual care was reported at 24 week follow-up (p=0.0017) with exercise-placebo participants reporting a better overall satisfaction with life (Refer to Table 4.5).

Table 4.5Effects of exercise therapy and exercise-placebo relative to usual care on psychological health outcomes

Psychological health outcomes		Follow-up (weeks)							
		8 (mean diff, 95% CI)				24 (mean diff, 95% CI)			
		Mean	**lower**	**upper**	**Adj P[1]**	**mean**	**lower**	**upper**	**Adj P[1]**
Depression	Exercise therapy versus usual care	**-6.01**	-10.21	-1.81	**0.001**	**-4.49**	-8.78	-.0.20	**0.035**
	Exercise-placebo versus usual care	**-5.66**	-9.76	-1.55	**0.001**	**-4.98**	-9.14	-0.81	**0.009**
Total fatigue	Exercise therapy versus usual care	-1.13	-2.36	0.09	0.085	-0.68	-2.04	0.68	0.694
	Exercise-placebo versus usual care	**-1.25**	-2.44	-0.05	**0.037**	-1.15	-2.48	0.18	0.128
Satisfaction with life (SWL)	Exercise therapy versus usual care	0.72	-0.61	2.04	0.617	0.98	-0.38	2.35	0.2985
	Exercise-placebo versus usual care	0.35	-0.94	1.65	0.967	1.83	0.50	3.15	**0.0017**

[1] Paired comparisons between groups at each time point were adjusted by the Tukey-Kramer method

4.8 PHYSICAL SELF-PERCEPTIONS

A significant mean difference for physical conditioning competence in favour of exercise-therapy relative to usual care was recorded at both eight week ($p=<0.001$) and 24 week follow-up ($p=0.004$), there was however a reduction in effect at 24 week follow-up. The physical self-worth (PSW) subscale at eight week follow-up also showed a significant difference between exercise therapy and usual care ($p=0.03$). A similar significant mean difference was also recorded for the physical self–worth subscale scores between exercise-placebo and usual care at eight week follow-up ($p=0.005$). (Refer to Table 4.6).

4.9 BOOTSTRAPPING OF TRIAL OUTCOMES

It should be noted that the variables PWB, SWB, SWL, 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.

Table 4.6 Effects of exercise therapy and exercise-placebo relative to usual care on physical self-perceptions

Psychological health outcomes		Follow-up (weeks)							
		8 (mean diff, 95% CI)				24 (mean diff, 95% CI)			
		Mean	**lower**	**upper**	**Adj P[1]**	**mean**	**lower**	**upper**	**Adj P[1]**
Physical conditioning competence	Exercise therapy versus usual care	**0.60**	0.25	0.96	**<0.001**	**0.46**	0.11	0.82	**0.004**
	Exercise-placebo versus usual care	0.34	-0.00	0.69	0.054	0.33	-0.02	0.68	0.081
Attractiveness of body	Exercise therapy versus usual care	0.28	-0.02	0.59	0.086	0.27	-0.04	0.58	0.132
	Exercise-placebo versus usual care	0.15	-0.15	0.46	0.693	0.20	-0.11	0.50	0.425
Physical strength competence	Exercise therapy versus usual care	0.32	-0.05	0.68	0.131	0.33	-0.04	0.71	0.117
	Exercise-placebo versus usual care	0.24	-0.12	0.61	0.373	0.26	-0.11	0.62	0.313
Physical self-worth	Exercise therapy versus usual care	**0.49**	0.12	0.86	**0.003**	0.27	-0.10	0.65	0.286
	Exercise-placebo versus usual care	**0.47**	0.10	0.83	**0.005**	0.35	-0.02	0.72	0.069
Sports competence	Exercise therapy versus usual care	0.29	-0.04	0.62	0.124	0.19	-0.15	0.52	0.604
	Exercise-placebo versus usual care	0.24	-0.09	0.57	0.285	0.22	-0.11	0.56	0.382

[1] Paired comparisons between groups at each time point were adjusted by the Tukey-Kramer method.

4.10 THEORY OF PLANNED BEHAVIOUR (TPB) OUTCOMES

4.10.1 INTENTION

Analyses revealed a significant effect for intention between exercise therapy relative to usual care ($p=0.011$) at eight week and 24 week follow-up ($p=0.004$). A similar significant effect was reported for exercise-placebo relative to usual care ($p<0.001$) at eight week follow-up but not extending beyond that. A significant favourable effect for the variable of attitude was reported between exercise-placebo and usual care at eight week and 24 week follow-up respectively ($p=0.001$) and ($p=0.005$). Exercise therapy participants did not report any significant effect with regard to the outcome of attitude. (Refer to Table 4.7 for the effects of exercise-therapy and exercise-placebo relative to usual care on the TPB outcomes).

4.10.2 SUBJECTIVE NORM

There was evidence of a significant positive effect regarding subjective norm for exercise-placebo relative to usual care at 24 week follow-up.

4.10.3 PERCEIVED BEHAVIOURAL CONTROL

A significant mean difference in perceived behavioural control between exercise–placebo and usual care was evident at eight week follow-up ($p=0.046$), with exercise-placebo participants recording higher mean differences relative to usual care than exercise therapy participants.

4.10.4 ATTITUDE

The only significant difference between mean attitude scores was observed for exercise-placebo relative to usual care at eight week follow-up ($p=0.001$) and 24 week follow-up ($p=0.005$).

Table 4.7 Effects of exercise therapy and exercise-placebo relative to usual care on TPB variables

Psychological health outcomes		Follow-up (weeks)							
		8 (mean diff, 95% CI)				24 (mean diff, 95% CI)			
		Mean	**lower**	**upper**	**Adj P[1]**	**mean**	**lower**	**upper**	**Adj P[1]**
Intention	Exercise therapy versus usual care	**0.98**	0.15	1.82	**0.011**	1.10	**0.24**	1.96	**0.0046**
	Exercise-placebo versus usual care	**1.36**	0.55	2.18	**0.000**	0.81	-0.03	1.65	0.0640
No of times intention	Exercise therapy versus usual care	0.52	-0.08	1.12	0.133	0.57	-0.03	1.16	0.0749
	Exercise-placebo versus usual care	0.47	-0.09	1.04	0.154	0.34	-0.24	0.92	0.5262
Subjective norm	Exercise therapy versus usual care	0.50	-0.28	1.28	0.426	0.77	-0.03	1.58	0.0682
	Exercise-placebo versus usual care	0.76	-0.01	1.53	0.053	0.91	**0.12**	1.71	**0.0149**
Perceived behavioural control (PBC)	Exercise therapy versus usual care	0.58	-0.20	1.35	0.263	0.62	-0.17	1.41	0.2093
	Exercise-placebo versus usual care	**0.77**	0.01	1.53	**0.046**	0.56	-0.21	1.34	0.2875
Attitude	Exercise therapy versus usual care	0.28	-0.06	0.62	0.181	0.24	-0.11	0.59	0.3339
	Exercise-placebo versus usual care	**0.48**	0.14	0.81	**0.001**	0.43	**0.09**	0.77	**0.0054**

[1] Paired comparisons between groups at each time point were adjusted by the Tukey-Kramer method.

4.11 PHYSIOLOGICAL HEALTH OUTCOMES

Evidence of significant differences in mean aerobic fitness scores were recorded between exercise therapy and usual care (p=0.002) and exercise-placebo and usual care (p=0.021) at eight week follow-up. The greatest difference was recorded between exercise therapy and usual care. There were no other significant mean differences for either group relative to usual care for the physical outcomes of BMI, percentage body fat, weight, shoulder function, systolic and diastolic blood pressure. The variable of peak torque relative to bodyweight for the quadriceps was the only muscle function variable to reach statistical significance at eight week follow-up (p=0.020) favouring exercise-placebo relative to usual care.

See Table 4.8 for the effects of exercise therapy and exercise-placebo relative to usual care on physiological outcomes. Estimates of effect sizes expressed in units of 1 standard deviation for selected outcomes are presented for exercise-therapy relative to usual care and exercise-placebo relative to usual care are displayed in Figure 4.1 and Figure 4.2 respectively.

Table 4.8 Effects of exercise therapy and exercise-placebo relative to usual care on physiological health outcomes

Physical health outcomes		Follow-up (weeks)							
		8 (mean diff, 95% CI)				24 (mean diff, 95% CI)			
		Mean	**lower**	**upper**	**Adj P[1]**	**mean**	**lower**	**upper**	**Adj P[1]**
BMI	Exercise therapy versus usual care	-0.09	-0.75	0.57	0.999	-0.03	-0.72	0.65	0.999
	Exercise-placebo versus usual care	-0.17	-0.81	0.48	0.975	-0.30	-0.97	0.37	0.791
Percentage body fat	Exercise therapy versus usual care	0.24	-1.94	2.41	0.999	-0.33	-2.67	2.01	0.998
	Exercise-placebo versus usual care	0.64	-1.48	2.76	0.951	-0.75	-3.01	1.50	0.927
Aerobic fitness (ml/kg/min)	Exercise therapy versus usual care	**2.89**	0.78	4.99	**0.002**	1.24	-0.98	3.45	0.583
	Exercise-placebo versus usual care	**2.25**	0.22	4.28	**0.021**	0.98	-1.16	3.13	0.761
Systolic blood pressure	Exercise therapy versus usual care	1.56	-8.65	11.78	0.997	-3.34	-14.2	7.53	0.9470
	Exercise-placebo versus usual care	2.14	-7.70	11.98	0.988	-2.99	-13.35	7.37	0.9593
Diastolic blood pressure	Exercise therapy versus usual care	-1.29	-6.38	3.81	0.977	-0.98	-6.39	4.44	0.9950
	Exercise-placebo versus usual care	-0.07	-4.99	4.84	1.000	-0.04	-5.21	5.13	1.0000
Shoulder function	Exercise therapy versus usual care	-1.63	-3.81	0.56	0.264	-0.96	-3.21	1.28	0.8112
	Exercise-placebo versus usual care	-1.38	-3.52	0.77	0.426	-1.51	-3.71	0.69	0.3548

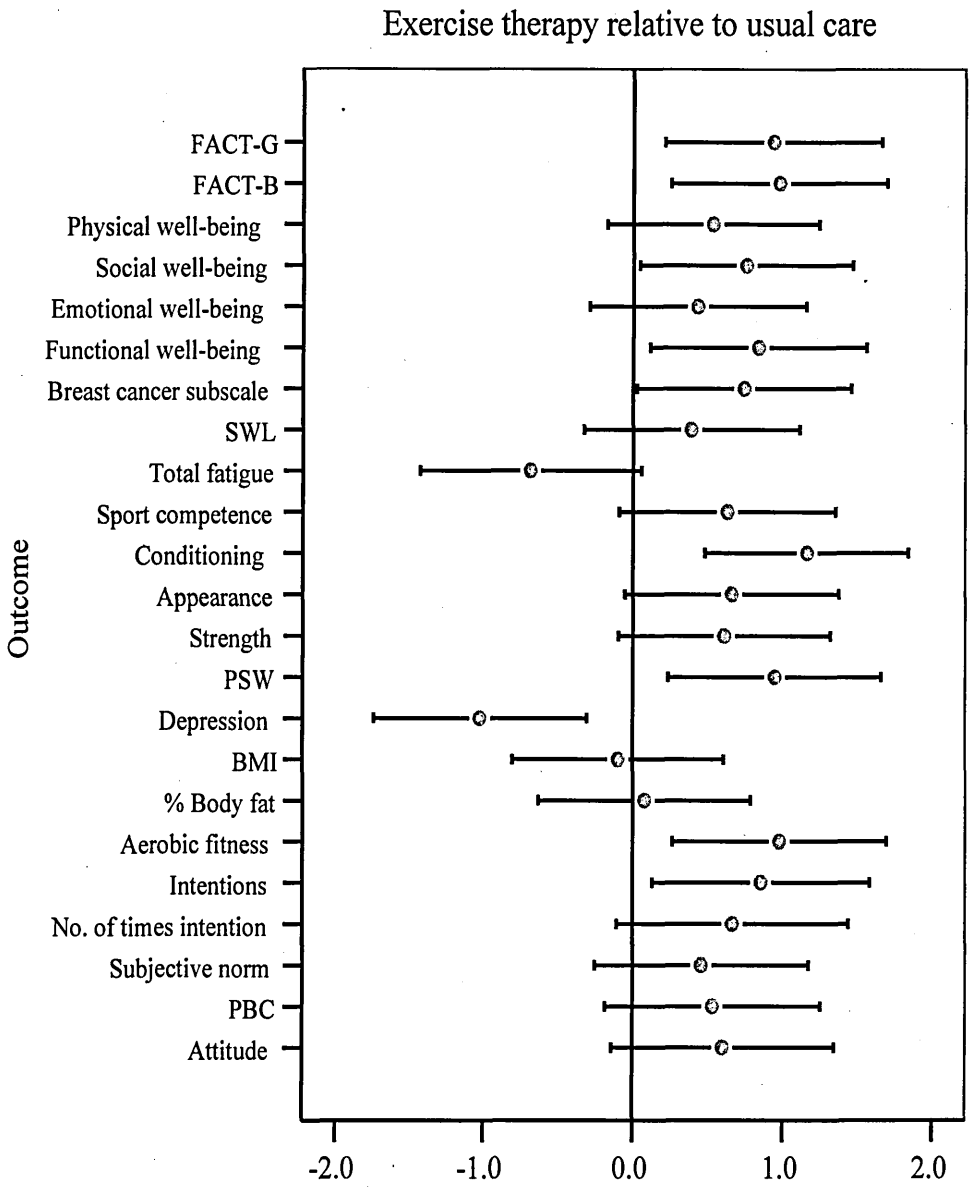
[1] Paired comparisons between groups at each time point were adjusted by the Tukey-Kramer method

Table 4.8 continued Effects of exercise therapy and exercise-placebo relative to usual care on physiological health outcomes

Physical health outcomes		Follow-up (weeks)							
		8 (mean diff, 95% CI)				24 (mean diff, 95% CI)			
		Mean	lower	upper	Adj P[1]	mean	lower	upper	Adj P[1]
Quadriceps peak torque	Exercise therapy versus usual care	2.26	-5.16	9.67	0.946	-1.83	-9.82	6.15	0.9839
	Exercise-placebo versus usual care	6.48	-0.78	13.73	0.106	3.88	-3.61	11.38	0.649
Quadriceps peak torque/bodyweight	Exercise therapy versus usual care	6.38	-4.79	17.55	0.550	-1.70	-14.4	11.03	0.998
	Exercise-placebo versus usual care	**12.21**	1.23	23.19	**0.020**	7.19	-4.46	18.84	0.465
Quadriceps total work	Exercise therapy versus usual care	59.95	-161.3	281.22	0.967	-81.69	-331	168.2	0.9286
	Exercise-placebo versus usual care	164.01	-53.14	381.16	0.243	131.62	-97.7	361.0	0.5459
Hamstrings peak torque	Exercise therapy versus usual care	2.27	-2.19	6.73	0.667	0.76	-4.38	5.90	0.9980
	Exercise-placebo versus usual care	1.55	-2.82	5.92	0.900	2.68	-1.97	7.34	0.5400
Hamstrings peak torque/bodyweight	Exercise therapy versus usual care	4.85	-2.43	12.13	0.377	1.78	-6.70	10.27	0.9893
	Exercise-placebo versus usual care	4.75	-2.31	11.81	0.366	6.22	-1.35	13.78	0.1669
Hamstrings total work	Exercise therapy versus usual care	55.25	-61.92	172.41	0.733	18.79	-114	151.7	0.9983
	Exercise-placebo versus usual care	61.09	-53.05	175.23	0.617	88.51	-32.25	209.2	0.2729

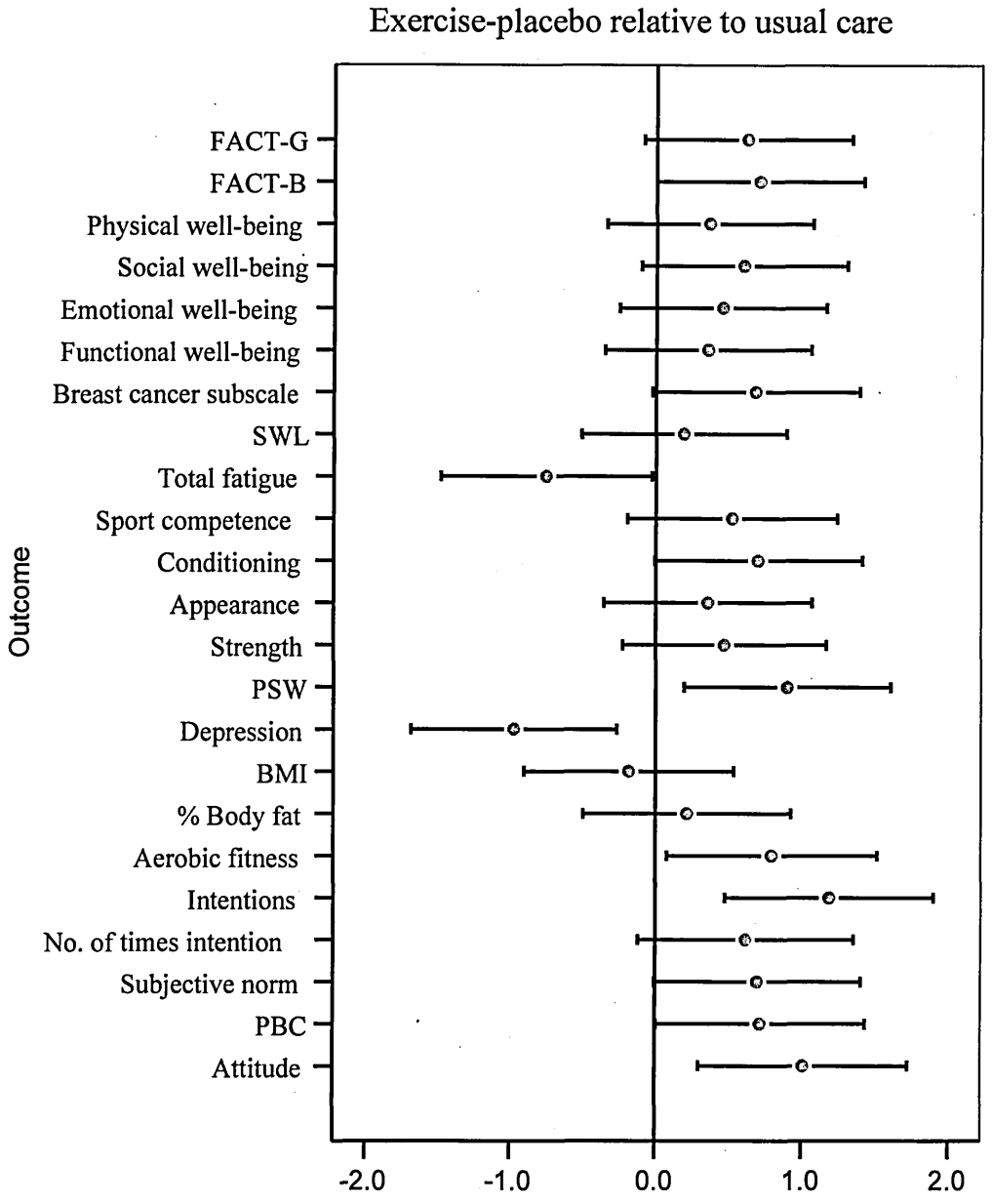
[1] Paired comparisons between groups at each time point were adjusted by the Tukey-Kramer method

Figure 4.1 Estimates of effect sizes for exercise therapy relative to usual care on selected outcomes



Effect estimates with 95% confidence intervals for the difference (adjusted for baseline scores) between exercise-therapy relative to usual care at eight week follow-up. Estimates expressed in units of 1 standard deviation.

Figure 4.2 Estimates of effect sizes for exercise-placebo relative to usual care on selected outcomes



Effect estimates with 95% confidence intervals for the difference (adjusted for baseline scores) between exercise-placebo relative to usual care at eight week follow-up. Estimates expressed in units of 1 standard deviation.

4.11 PHYSICAL ACTIVITY

There was a significant difference between the percentage of participants in the exercise therapy group relative to usual care who increased their physical activity to at least three times a week at both eight week follow-up ($p<.001$) and at 24 week follow-up ($p< .001$). This was also the case for exercise-placebo relative to usual care at eight week follow-up ($p<.001$) and 24 week follow-up ($p<.001$) although exercise-placebo reported less exercise than exercise therapy. A greater proportion of exercise therapy participants moved to the action or maintenance stage of change (SOC) for exercise compared with usual care at 24 week follow-up. A similar effect between exercise-placebo and usual care ($p=.03$) was also recorded (Refer to Table 4.9)

Table 4.9 Intervention effects upon physical activity and stage of change for exercise

	Follow Up (weeks)			
	8		24	
Intervention	**No. of patients**	**%**	**No. of patients**	**%**
Physical activity*				
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**				
Exercise therapy	-		16 of 31	52
Exercise-placebo	-		10 of 34	29
Usual care	-		2 0f 31	6

* Analyses were performed comparing the percentages of patients that reported a change from being inactive at baseline (i.e. 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 assess behaviour change over a period of six months. Analyses were performed comparing the percentages of patients that reported a change from being at risk (i.e. pre-contemplation, contemplation, and preparation) at baseline to being in the action or maintenance stages of change at follow-up between the groups.

4.12 COMPLETION OF ASSESSMENTS

Follow-up was achieved on 93% of participants at eight week follow-up and 89% at 24 week follow-up. Little's D Test indicated that missing data were missing completely at random (χ=88.2, df=1,290, p=0.99) therefore there was no evidence of disproportionate drop-out from the groups.

4.13 ADHERENCE TO INTERVENTIONS

Adherence was calculated on the basis of session participation achieved by the participants. The amount of exercise achieved by participants (i.e. duration, rating of perceived exertion and heart-rate) was calculated by drawing data from the physical activity logs that were recorded and maintained by the research assistants. 77% of the exercise therapy group attended 70% of the prescribed exercise sessions. A slightly higher proportion of exercise-placebo participants 88.9%, attended 70% of the prescribed exercise sessions. Chapter 7 provides more detailed information regarding the exercise adherence of the participants in this study.[183]

CHAPTER 5. DISCUSSION

This is the first RCT study conducted in the UK to investigate the effects of exercise therapy upon QoL in previously sedentary women who had been treated for breast cancer. In response to concerns that improvements in QoL may be attributable to the increased attention given to cancer patients during exercise interventions, this study uniquely included an equal contact exercise-placebo (attention-control) group. The primary aim of this study was to examine the effects of exercise therapy upon QoL, and secondary aims included the investigation of the effects of exercise therapy upon psychological well-being outcomes and selected measures of physical function.

5.1 THE EFFECTS OF EXERCISE THERAPY UPON QOL

The primary finding of this study was in support of the hypothesis which stated that an eight week supervised exercise intervention would lead to favourable changes in exercise therapy participants' QoL. The exercise therapy group reported significantly higher QoL scores relative to usual care at eight week follow-up, by a magnitude of 9.8 units as measured by the FACT-G scale. A minimally important difference in cancer patient's QoL has been reported to be a 5-6 units on this scale.[184] The magnitude of effect achieved by the exercise therapy group relative to usual care, exceeded the minimally important difference threshold by some distance. This is particularly encouraging as improvement of QoL in cancer patients is a current goal of cancer management.[185] The positive results regarding QoL are not thought to be attributable to any attention effects arising from the interaction between the research assistant and participants; as the exercise-placebo (attention-control group) who received equal amounts of contact time did not report QoL benefits that were of statistical significance. However, it is worth considering that attention effects may have influenced findings in previous trials that included supervised exercise sessions. The QoL findings found in

this study here are in accordance with four, [110,112,117,120] of the six exercise [110-112,117,120,123] RCT's that have found significant improvements in global QoL in women treated for breast cancer. In light of this study's findings, QoL in this population does appear amenable to intervention and supervised aerobically-based exercise therapy would seem to offer an effective strategy to achieve this.

Current approaches to improving QoL in cancer patients have tended to focus upon psycho-social support therapies such as informational and education interventions, coping skills and social support interventions. However these types of approaches do not address the physical and functional concerns that breast cancer patients have, after completion of treatment.[186] Furthermore, the observed treatment effect sizes have been reported to be relatively small [68] thereby raising questions about their utility and the potential for bias.[187] It should be noted that the significant improvement in overall QoL in this study was only short-term, and did not extend to later follow-up. This finding suggests there is a need for researchers to better support individuals in making the transition from supervised, one-to-one exercise participation to independent regular exercisers.

5.2 THE IMPACT OF EXERCISE THERAPY ON SPECIFIC COMPONENTS OF QOL.

A noteworthy finding of this study was that there was a significant effect for the functional well being (FWB) domain of QoL, favouring exercise therapy relative to usual care at eight week follow-up. This sub-component of QoL has been highlighted as one of the most important dimensions of QoL in breast cancer patients [70,76] during treatment and after treatment. Of interest here is that despite being at least 12 months post-treatment, women in the exercise therapy group were still able to benefit from participation in an exercise intervention. This is reassuring as FWB encompasses an

individual's capacity to work (with reference to both paid employment and home), ability to enjoy activities and feel content with their QoL. Indeed FWB may be one of the key elements that enable women to make the transition back to their normal routine, a key aspiration of women who have been treated for breast cancer.[71]

Significant differences were found favouring exercise therapy relative to usual care for social well-being (SWB) and the breast cancer specific subscale (BCS) (which constitutes psychological and physical concerns related to breast cancer diagnosis and treatment). In this study the exercise therapy group recorded a mean difference of 13.1 units on the FACT-B scale relative to usual care, demonstrating the considerable merits of supervised aerobically-based exercise interventions. Research by Courneya et al [110] also found that women who participated in a supervised 15-week cycling intervention recorded a mean difference of 9.1 units relative to usual care on the FACT-B scale. In the current study the exercise therapy group recorded a mean difference of 13.1 units on the FACT-B scale relative to usual care, demonstrating the considerable merits of supervised aerobically-based exercise interventions.

Recent studies have demonstrated that activities not based on aerobic exercise, such as those that focus on movement like dance, [188] Yoga [189] and Tai Chi Chuan [112] can significantly improve QoL and psychological well-being in breast cancer patients. This type of exercise modality warrants future investigation as it may broaden the range of therapeutic exercise interventions available to patients.

5.3 PSYCHOLOGICAL HEALTH OUTCOMES

5.3.1 DEPRESSION

Depression scores were significantly lower in both the exercise therapy and exercise-placebo groups relative to usual care at both eight week and 24 week follow-ups. The beneficial effect of exercise therapy upon the outcome of depression concurs

with the findings of a study by Segar et al [122] which investigated a 10-week aerobic based exercise intervention in breast cancer patients post-treatment. Segar et al [122] reported exercisers significantly reduced their levels of depression by 44% compared to a non-exercise control comparison. The present study also found that participants who engaged in the exercise-placebo intervention also reported reduced depression relative to usual care, this finding is in contrast to a resistance training study conducted by Ohira et al [120] in breast cancer patients that did not report any changes in depression. The results from this study with regard to the outcome of depression add to the very limited evidence-base for this particular outcome, further research investigating the efficacy of exercise rehabilitation in reducing depression in breast cancer patients is warranted.

5.3.2 FATIGUE

Despite considerable evidence [20,37,43] suggesting that fatigue is a persistent, long-term side effect of cancer treatment and calls to implement exercise interventions to manage cancer-related fatigue, [50] this study found no significant effect of moderate intensity exercise therapy relative to usual care on indices of fatigue. This finding is in contrast to a comparable post-treatment aerobic exercise based study [110] that found significant reductions in symptoms of fatigue in post-menopausal women who had completed their treatment 14 months previously. The present finding is in support of the other two post-treatment exercise RCT's that have investigated fatigue, and similarly did not find any significant reductions in fatigue.[118,123] An unanticipated finding of this study was that the exercise-placebo group did report a statistically significant (at eight weeks) reduction in fatigue compared to usual care. This improvement in fatigue symptoms did not however, persist at 24 week follow-up. This favourable finding may suggest that there may be mechanisms specific to the kind of light intensity exercises undertaken in the exercise–placebo that positively mediates perceptions of fatigue.

There is a greater body of evidence confirming the positive role of exercise in managing fatigue during breast cancer treatment [36,48,49,114,127,162,190] this may be because the severity of fatigue is greater during active treatment than post-treatment. Given the observation that cancer-related fatigue is not alleviated by rest [20] it would be wise to further pursue the area of the aetiology of cancer related fatigue and the efficacy of exercise interventions in its treatment.

5.3.3 PHYSICAL SELF-PERCEPTIONS

A moderate intensity exercise therapy programme was able to facilitate improvements in physical self-perceptions in women treated for breast cancer. The participants in the exercise therapy intervention reported significantly better physical conditioning competence relative to usual care at eight week follow-up and this effect was still evident at 24 week follow-up. With this in mind, it appears that the participants in the exercise therapy group had the opportunity to achieve a degree of exercise mastery and competence which are thought to underpin positive physical self-perception. [158] This may have been due to the uncomplicated nature of the exercises undertaken such as walking and stationary cycling and the tolerable, moderate intensity at which they were performed. General physical self-worth was also reported to be significantly higher in the exercise therapy group relative to usual care; this was also the case for the exercise-placebo group relative to their usual care counterparts. However the magnitude of effect for general physical self-worth was greater for exercise therapy participants relative to usual care than exercise-placebo participants relative to usual care. Mastery experiences associated with an exercise programme could explain the more positive feelings of physical self-worth reported by participants in the exercise therapy intervention. The use of exercise therapy to promote feelings of positive self-worth might be particularly appropriate given that women treated for breast cancer

report diminished physical function.

5.3.4 THEORY OF PLANNED BEHAVIOUR VARIABLES

Previous research [137,170,191,192] with breast cancer patients has examined the predictive ability of the components of theory of planned behaviour (TPB) variables and have found associations between attitudes, perceptions of perceived behavioural control, intentions and subjective norms and exercise motivation and adherence.[136-138] A significant difference between exercise therapy and usual care was observed for intention toward maintaining exercise at both eight week and 24 week follow-up. The exercise counselling strategies in the study offered exercise therapy participants the opportunity to cognitively reappraise the value and importance of exercise in their lives. This type of approach may have helped women to strengthen their commitment towards sustaining their exercise participation and this is reflected in their higher intention to exercise scores at 24 week follow-up. Perceived behavioural control and attitude were not significantly affected by the exercise therapy intervention compared to usual care. Interestingly, the exercise–placebo intervention did report significant higher perceived behavioural control and attitude scores relative to usual care at both follow-ups. It might be that the participants in the exercise-placebo group were initially unfamiliar with the type of muscular toning and flexibility exercises performed and consequently over the eight week intervention were able to increase their feelings of exercise competence.

5.4 PHYSICAL OUTCOMES

No significant effects were observed for the outcomes of body composition, bodyweight or BMI. It is not surprising this study failed to observe significant effects of exercise therapy intervention on body composition, bodyweight or BMI given the current study was of a relatively short duration and it did not include any dietary intervention such as calorie restriction. Increases in body weight and body composition

over the course of treatment for cancer have been reported to be a key concern for women treated for breast cancer.[193,194] In line with findings from this study recent systematic review [84,102] evidence based on exercise RCT's with breast cancer patients has not revealed any clinically or statistically significant changes in bodyweight, body composition or BMI. Only a few studies to date have focussed their endpoints on changes in weight and body composition, thus the evidence base is both sparse and vague.[84] As such it is recommended that future trials adopt bodyweight and composition changes as primary outcomes and employ more precise and accurate methods of assessment.

Both exercise therapy and exercise placebo groups were able to improve their aerobic fitness at eight weeks follow-up relative to the usual care group. Similar beneficial cardio-respiratory fitness effects were seen in a pilot study of women 2-5years post-breast cancer surgery who attended an eight week combined aerobic and resistance training intervention.[117] It is somewhat unexpected that the exercise–placebo group increased their aerobic fitness given the nature of the exercises that were performed. Interestingly, a trial conducted by Courneya et al [127] that compared psychotherapy with psychotherapy plus exercise, found that the psychotherapy group alone also improved their cardio-respiratory fitness. One explanation for the improvement in aerobic fitness in the exercise-placebo group could be that the exercise-placebo group increased their exercise competence and this might have given women the impetus to be aerobically more active outside of the trial.

5.5 PHYSICAL ACTIVITY

The exercise therapy and exercise–placebo intervention groups proved successful in improving levels of physical activity relative to usual care at eight week and 24 week follow-up. Improvements were also observed for stage of change of

exercise (SOC) at eight week and 24 weeks for both exercise intervention groups. The magnitude of change in physical activity and SOC was greater for exercise therapy participants compared to the other trial groups. This is encouraging as it may reflect the benefit of the exercise counselling approach which aimed to help participants in the exercise therapy group to cognitively appraise their exercise participation and consider ways to sustain their participation over time.

5.6 LIMITATIONS AND STRENGTHS

Blinding of outcome assessments was not possible in this study, however this was not considered a potential source of bias regarding the primary outcome measure as this was a self-report instrument. It is possible that there may have been the opportunity for experimenter effects relating to the assessment of aerobic fitness and muscle function. Standardised protocols were followed and the research assistant was mindful of keeping all verbal and non-verbal cues constant across all participant assessments. A total of 108 patients were randomised in to this study, although the sample size calculations indicated that 114 patients were required. Therefore this trial is marginally underpowered. Despite this, it was still possible to report a significant effect of the magnitude expected for the primary outcome in favour of exercise therapy. Several outcomes were measured throughout the course of the study and despite adjusting for paired comparisons, there may be the potential for a type I error to exist due to multiple testing.

The inclusion of an exercise-placebo (attention-control) arm is considered a significant methodological improvement on previous research. A further strength of this study is that adherence rates were good, 77% of participants allocated to exercise therapy intervention and 88.9% of participants allocated to the exercise–placebo intervention attended 70% of prescribed exercise sessions.

5.7 CONCLUSIONS

This study has demonstrated that previously sedentary women treated for breast cancer in the UK, who took part in an eight week one-to-one supervised exercise therapy intervention, were able to achieve clinically important, short-term benefits in their QoL. Furthermore attention effects did not appear to be responsible for the improvement in the primary outcome of QoL. Modest improvements in psychological well-being outcomes and aerobic fitness were also positively associated with aerobic exercise therapy. The findings from this RCT study make a notable contribution to the limited body of evidence that currently exists, regarding the role of exercise in improving QoL in breast cancer patients who have completed their treatment. This study demonstrated that women treated for breast cancer can engage in moderate aerobic exercise. This is particularly encouraging in the light of recent evidence [93] that reports an association between moderate levels of aerobic physical activity and a reduction in the risk of disease recurrence in women treated for breast cancer.

CHAPTER 6. RECRUITMENT

6.1 INTRODUCTION

Recent systematic review evidence suggests that exercise rehabilitation for cancer patients may provide significant physiological and psychological benefits both during and post cancer treatment.[105,107] However, it has been recommended that future intervention studies should adopt randomised controlled designs to help establish the range and magnitude of the potential beneficial effects for cancer patients.[95,104,108] Patient recruitment into randomised controlled trials (RCT) is recognised to be one of the most challenging and time consuming elements of the study process. It has been reported that it is often necessary to extend the time allocated for trial recruitment beyond originally planned timescales.[195] Failure to recruit a sufficient number of participants can compromise the statistical power of a trial limiting the strength of the study to detect intervention effects. This can result in a biased sample which subsequently can jeopardise the external validity of the trial.[108,196] Indeed, "Project Lead" a lifestyle intervention study for older breast and prostate cancer patients [197] did not meet its recruitment target of 420 participants; it recruited less than half the anticipated number of participants (n=182) resulting in a statistically underpowered trial. Ott and colleagues [198] were faced with similar recruitment difficulties in recruiting breast cancer patients to a RCT for osteoporosis prevention. The authors had to restructure their recruitment resources and strategies two thirds of the way through their recruitment phase to meet their accrual goals. Recruitment into RCT's presents an ongoing challenge to identify and reach all potentially eligible patients who may benefit from the intervention.

Whilst a number of breast cancer trials have been published, to date, no study has documented recruitment into an exercise therapy RCT of women treated for breast

cancer in the UK. Patient attributes, including socio-economic and demographic characteristics, may influence willingness to participate in a RCT. Previous research has not fully explored the possible differences in the characteristics of responders and non-responders to exercise trials involving breast cancer patients, yet as highlighted earlier, this information can be an important source of bias that must be considered when assessing the validity and generalisability of trial results. Potentially, patients recruited by different methods and subsequently randomised into a trial may vary significantly in terms of their socio-economic characteristics, lifestyle behaviours or the type of cancer treatment received.[108] Specifically, cancer patients who respond to community advertisements to take part in lifestyle and behavioural change interventions, may be younger and more motivated than patients recruited from more traditional health settings such as hospitals health services. An alternative explanation for willingness to enrol into a trial is put forward by Berglund and colleagues [199] who suggest that cancer patients who choose to participate in such trials may be expressing a need for support in the rehabilitation process.

This chapter aims to provide an overview of the effectiveness of different recruitment strategies used to recruit participants to an eight week RCT designed to investigate the effects of exercise therapy on quality of life (QoL) and associated measures in sedentary women treated for breast cancer. Furthermore this chapter provides descriptive statistics for the different strategies that were used to recruit potentially eligible women to the study. Differences in the characteristics of responders and non-responders to clinician postal invitations to participate in the trial are also reported. An examination of the associations between trial recruitment routes and patient socio-demographic characteristics, lifestyle behaviours and breast cancer treatment regimens is also provided.

6.2 METHODS

Detailed descriptions of the methods and interventions for this study have been provided in Chapter 3. In brief, this study aimed to recruit at least 36 women to either an exercise therapy, exercise-placebo group or usual care. Recruitment into the trial began in January 2003 and closed in July 2005 (30 months).

6.2.1 RECRUITMENT STRATEGIES AND ELIGIBILITY

6.2.2 CLINICIAN INVITATION LETTERS

The primary recruitment strategy for the study was by postal invitation letter from the patients' treating oncologist or surgeon (referred to as clinician invitation). Treating oncologist or surgeons from collaborating hospitals in South Yorkshire, United Kingdom (UK) identified potentially eligible patients from hospital records. Clinician invitation letters were accompanied by a trial information sheet which briefly outlined the aims of the study. Four out of six oncologists and surgeons agreed to assist with recruitment by writing to their eligible patients. Letters were sent in batches of approximately 15-30 throughout the trial recruitment period to allow the number of participant cohorts to be effectively managed. Clinician invitation letters were only sent to women aged 18-65 years who were one to three years post treatment and who had been treated at collaborating hospitals in South Yorkshire. Women with metastases and inoperable or active loco-regional disease were ineligible and therefore not invited to participate. No attempt was made to further contact patients who did not respond to the invitation from their clinician to participate in the study.

6.2.3 COMMUNITY STRATEGIES

Secondary recruitment strategies involved media (television, radio and press) advertisements, word of mouth, presentations and trial awareness activities to cancer support groups and breast cancer nurses. The study launch was supported by both

television and radio press releases. Throughout the recruitment period members of the research team gave interviews to the local and regional newspapers and magazines; these tended to appear in conjunction with other cancer events that were happening regionally and nationally, for example breast cancer awareness month and Race for Life events. A three-minute feature about the study was aired on regional BBC television news programmes on four occasions (including prime time) over one day, approximately half-way through the trial recruitment period.

In an attempt to reach as many participants as possible posters and leaflets that described the purpose of the trial with contact information were delivered to various community settings such as supermarket checkouts, GP surgeries, cafes, shopping venues and libraries. Participants were encouraged to tell friends and family about the study and asked to pass on the research team's contact details to any other potentially eligible participants they might know.

On five occasions throughout recruitment phase members of the research team made presentations to regional breast cancer care support groups and local organisations. Leaflets were also sent to breast cancer nurses at the start of the study requesting referral of potentially eligible patients. On two occasions, members of the trial team made presentations to breast cancer nurses and allied health professionals who were attending information/training events in the local area and requested that they publicise the study to potentially eligible patients. All trial literature, presentations and advertisements indicated that only sedentary women 18-65 years who were between 12-36 months post-treatment were eligible for the study. No other trial eligibility criteria were specified on trial literature.

Patients recruited via community strategies verbally reported information about their age, diagnosis and cancer treatment eligibility as outlined above. Letters to

potential patients treating oncologist/surgeon were sent to confirm this information. All recruitment strategies ran at the same time, so patients may have been made aware of the study by more than one recruitment method. Given this possibility, the recruitment strategy reported by patients when they first contacted the trial office to register their interest in participating in the study was documented. All patients had to be resident within the trial ethical approval catchment areas, to be eligible.

6.3 ELIGIBILITY SCREENING

For all recruitment routes, interested patients were prompted by clinician letter or community advertisements to contact the research team by calling a dedicated telephone line. Initial eligibility screening was conducted by telephone and in a few cases this was also conducted by e-mail at the request of the patient. The screening confirmed patients were indeed eligible according to their age, diagnosis and treatment criteria and their current exercise behaviour; (only sedentary women at the pre-contemplation, contemplation and preparation stages of change for exercise (SOC) [134] were eligible. During the telephone screening interested patients, deemed to be eligible were given an overview of the study, its purpose, potential time requirements and were made aware that the study was a RCT and as such they had a 33% chance of being allocated to one of the three trial groups. Patients had to be willing to attend exercise sessions three times per week to be eligible for the trial.

Patients still deemed eligible at this point were then invited to attend a familiarisation session at the University centre where the trial took place at a convenient time. This provided the opportunity for patients to meet with the trial researcher and to ask questions. During the familiarisation session which lasted approximately 45-60 minutes, a detailed description of the research study was given. This was guided by the patient information sheet. Potentially eligible patients were then further screened for

morbidities and contra-indications to exercise using the Physical Activity Readiness Questionnaire (PAR-Q).[155] Patients with co-morbidities that contra-indicated exercise participation (such as uncontrolled hypertension) were not automatically excluded at this stage but were asked to contact their general practitioner for further investigation and their approval to enter the study. Women who were not willing to accept randomisation to usual care or exercise-placebo intervention groups were not eligible for the trial. Patients were given contact details of the researcher in case patients had further questions they needed answering. Patients were subsequently invited to visit the trial Centre with their completed informed consent for their baseline assessment of outcomes, after which patients were randomised to one of the trial conditions (as described in chapter 3).

6.4 RECRUITMENT INCENTIVES

All patients were informed that a financial contribution towards travel expenses would be made. Randomised patients were reimbursed £2.50 towards their travel expenses for each visit they made to the study centre, this included both assessment and intervention visits. In addition, all randomised patients received a £20 sports shop voucher on completion of the intervention phase of the study.

As a recruitment incentive and to encourage compliance with follow-up assessments, it was explained to all patients at the familiarisation stage that if they were randomised to the usual care group they would be offered the opportunity to attend six "one-to-one" supervised exercise sessions at the Centre, free of charge upon completion of their final follow-up assessment of outcomes at 24 week follow-up.

6.5 MEASURES

At baseline all patients provided information concerning their medical history specific to their cancer diagnosis and treatment regimen, use and type of hormonal

therapies and the presence of lymphoedema. Body mass index (BMI), percentage body fat (using bioelectrical impedance), aerobic fitness (estimated $\dot{V}O_{2\,max}$) and stage of change for exercise [154] were also recorded. Recent physical activity behaviour was assessed by asking the question: 'How often have you participated in one or more physical activities for 20 to 30 minutes per session during your free time in the last 3 months?' Patients were asked to respond to one of a series of exercise frequencies: never, about once per month, about two or three times per month, about once per week, about twice per week, about three times per week and about four times or more per week. This method for assessing exercise behaviour is based on previous research [171,172] and has been used in studies with cancer patients [127,200]. To assess socioeconomic status The Index of Multiple Deprivation (IMD) [181] rank score was calculated for each patient.

6.6 DATA ANALYSES AND STATISTICAL METHODS

The randomisation yield by clinician invitation is based on the number of patients interested and randomised divided by the number of letters sent. For all other recruitment routes, randomisation yields are based on the number randomised divided by the number of interested responses. The estimated recruitment rate of eligible patients (total randomised divided by number interested and eligible) is based on the assumption that the trial eligibility rate for responders and non-responders would be the same. Those who did not respond to the clinician invitation letter and those who withdrew their interest after making an initial enquiry or were not further contactable were considered as a discrete group in this study as these women did not pursue an interest and willingness to enter the trial despite recruitment efforts made by the research team.

For analysis purposes the various community recruitment routes of cancer care

support groups/breast cancer nurses, media advertisements and word of mouth were combined into a single route of recruitment, which is referred to as community advert. Ranked data for IMD were converted to quartiles for analysis; quartile 1 represented the least deprived group and quartile 4 represented the most deprived. Patients current physical activity behaviour was categorised into one of four groups according to frequency of exercise reported (Never, ≤3 times per month, once per week and ≥twice per week).

Statistical analysis was performed to investigate whether responders and non-responders to clinician invitation letters differed by age and IMD, independent t-test and chi-squared tests were used respectively. In order to analyse the differences in randomised patients' characteristics according to their route of recruitment (i.e. clinician invitation letter or community advert) a series of independent t-tests (continuous variables) or chi-squared tests (dichotomous variables) were used. Due to multiple testing, $p<0.01$ was used to denote a significant difference between routes of recruitment and patients' characteristics.

6.7 RESULTS

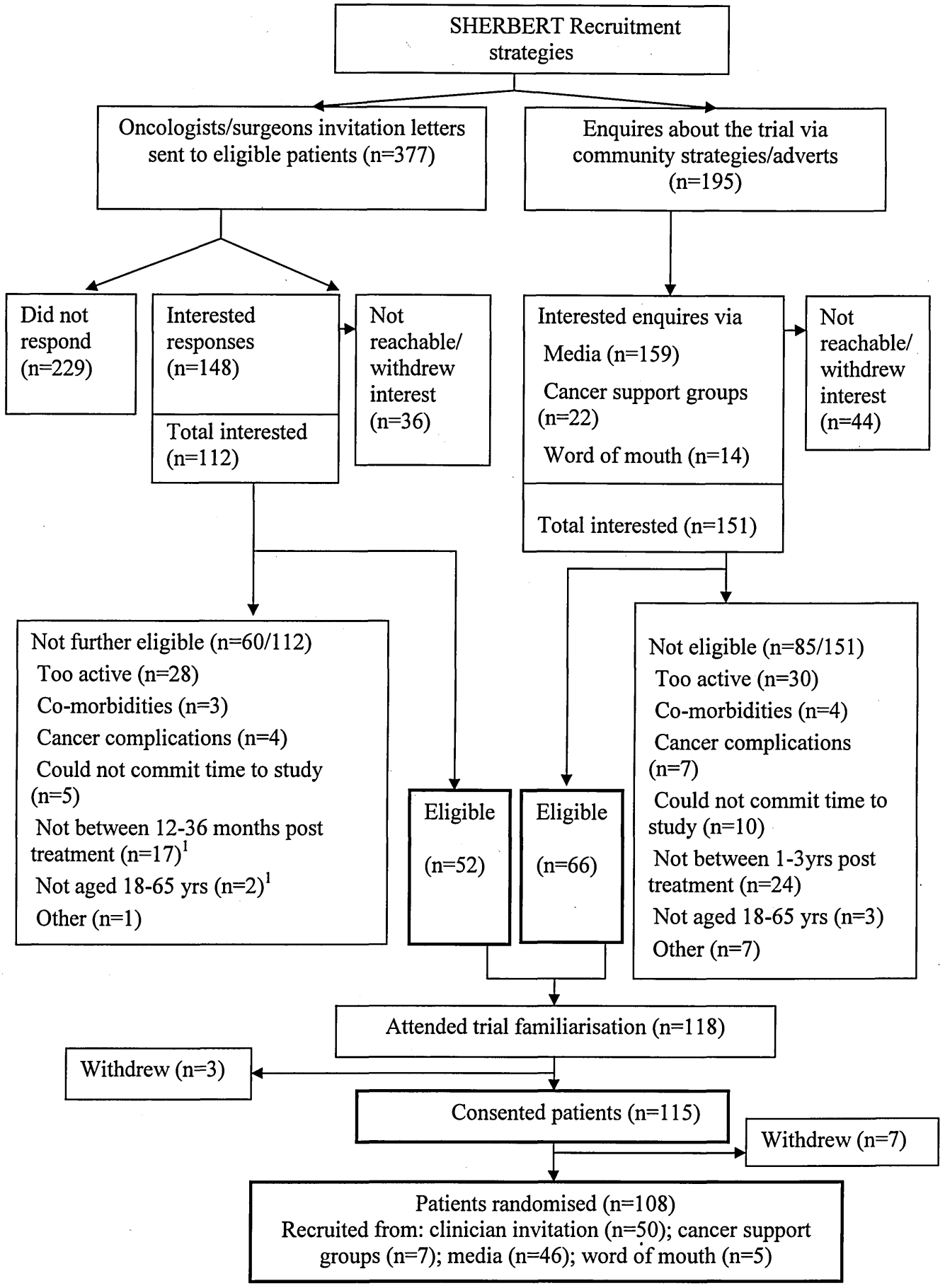
6.7.1 RESPONSE AND ELIGIBILITY RATES

In total, 572 interested patients were identified from all the trial recruitment strategies (see Figure 6.1). The response rate to clinician invitations was 39.3% (n=148/377), of these 24.3% (n=36/148) withdrew their interest or were not reachable by the research team after making an initial enquiry about the study. Thus, 112 patients who replied to clinician invitations remained interested and potentially eligible to take part in the trial. Community recruitment strategies elicited 195 enquiries in total. The respective contribution of community strategies/adverts sources was; media adverts (n=159); cancer care support groups (n=22) and word of mouth (n=14). 22.6% (n=44)

of patients who had enquired about the study via community strategies withdrew their interest/were not reachable after making initial contact with trial office. A total of 151 patients identified from community strategies remained interested and potentially eligible.

Of the patients interested in participating in the trial and recruited via oncologist invitation letter (n=112), 52 were considered eligible. For community adverts, of those patients that remained interested in the study (n=151), 66 were eligible See Figure 6.1 for an overview of patient recruitment into the study.

Figure 6.1 Patient recruitment into the study



Notes: [1]Some women delayed responding to their oncologist/surgeon invitations and were then subsequently ineligible to take part.

6.7.2 REASONS FOR INELIGIBILITY

Of patients who remained reachable and interested in the study, 145 were found to be ineligible after completing telephone screening. The reasons for ineligibility across recruitment strategies, in order of prevalence, were being too active (n=58/572, 10.1%), not between 12-36 months post treatment (n=41/572, 7.2%), not being able to commit to an exercise programme three times per week (n=15/572, 2.6%), cancer-related medical complications (n=11/572, 1.9%), co-morbidities that contra-indicated exercise participation (n=7/572, 1.2%), not aged 18-65 years (5/572, <1%) and other reasons (not living in ethical approval catchment areas and male) (8/572, 1.4%).

6.7.3 RANDOMISATION YIELDS

The randomisation yield (total randomised divided by number of letters sent) for clinician invitation letters was 13.3% (50/377). Randomisation yield rates for community recruitment strategies (total randomised divided by number of enquires) were 31.8% (7/22) (cancer support groups), 28.9% (46/159) (media) and 35.7% (5/14) (word of mouth). Overall, when all the community strategies were combined into one category of community advert, the randomisation yield was 29.7% (58/195) indicating a greater randomisation yield than the primary recruitment strategy of clinician invitations.

6.7.4 RECRUITMENT RATE BASED ON RECRUITMENT VIA CLINICIAN INVITATION

Of the patients who responded to clinician invitations and remained available and interested (n=112) 46.4% (n=52) were eligible to be randomised. Assuming a similar eligibility rate for non-responders and those not reachable after making initial contact with the trial office (i.e. 46.4% of 265), it is estimated that 123 of these patients would have been eligible had they been interested in taking part in the trial. Therefore,

a total of 175 patients were estimated to be potentially eligible (n=123 non-responders/not reachable but estimated to be eligible plus 52 eligible patients). Thus, on the basis that 175 patients were eligible and 50 patients recruited by clinician invitation were eventually randomised, the estimated trial recruitment rate amongst eligible patients in response to clinician invitation is 28.6% (n=50/175). The recruitment rate was based only on the clinician invitation letter because this was the only recruitment route for which denominator data was available.

6.7.5 RESPONDERS AND NON-RESPONDERS TO CLINICIAN INVITATION

With respect to responders and non-responders to clinician invitations there were no significant differences regarding age of responders (n=129, mean=52.4 years) and non-responders (n=221, mean=54.2 years). There was a non–significant trend for responders (n=132) to be more affluent than non-responders (n=216) (χ^2=9.80, p=0.02). (Numbers vary due to missing values).

6.7.6 CONSENTING AND RANDOMISED PATIENTS

A total of 118 patients were considered eligible after completing telephone screening. After attending the familiarisation session, three patients subsequently withdrew from the study, resulting in 115 patients providing informed consent. Of consenting patients, a further seven withdrew prior to randomisation. In total 108 patients (94% of consenting patients) were eventually randomised over a period of 30 months; equating to the recruitment of 3.6 patients per month. Of 108 randomised patients, 50 were recruited from clinician invitation letters and 58 from community strategies/adverts (7 from cancer care support groups, 46 from media activities and 5 from word of mouth)

6.7.7 ASSOCIATIONS BETWEEN ROUTE OF RECRUITMENT AND RANDOMISED PATIENT CHARACTERISTICS

No significant differences in socio-economic characteristics (IMD), demographic, lifestyle or variables related to cancer treatment were found between those patients recruited by clinician letter and those recruited by community adverts indicating that the different recruitment routes were not producing biased participant samples. (Refer to Table 6.1). Chi-squared tests were not performed for the variables of ethnicity, smoking status and number of children as $\geq$ 25% of cell frequencies were less than five.

Table 6.1 Socio-demographic status, lifestyle behaviours and breast cancer treatment regimens of randomised patients according to route of recruitment

	Clinician invitation letter (n=50) **Mean (95% CI) or n (%)**	**Community adverts (n=58)** **Mean (95% CI) or n (%)**
Age, years	51.2 (49.0-53.4)	50.9 (48.4-53.4)
Body mass index (kg/m^2)	29.0 (27.8-30.1)	28.2 (26.9-29.5)
Percentage body fat	40.8 (39.4-42.1)	40.0 (38.2-41.8)
Weight (kg) (n=106)	77.5 (73.2-80.3)	75.8 (71.6-78.0)
Maximal oxygen consumption (ml/kg/min) (n=102)	28.1 (27.6-29.9)	30.1 (28.6-31.9)
Smoking status		
Smoker	5 (10.2)	4 (6.9)
Non-smoker	44 (89.8)	54 (93.1)
Missing	1 (2.0)	0
Ethnicity		
White	50 (100)	56 (96.6)
Non White	0	2 (3.4)
Index of multiple deprivation		
Quartile 1 (least deprived)	11 (22.0)	14 (24.1)
Quartile 2	15 (30.0)	16 (27.6)
Quartile 3	13 (26.0)	16 (27.6)
Quartile 4 (most deprived)	10 (20.0)	12 (20.7)
Missing	1 (2.0)	0
Stage of change for exercise		
Pre-contemplation & contemplation	29 (58.0)	29 (50.0)
Preparation	21 (42.0)	29 (50.0)
Physical Activity		
Never	16 (32.0.)	14 (24.1)
≤3 times per month	16 (32.0)	15 (25.9)
Once per week	12 (24.0)	17 (29.3)
≥Twice per week	6 (12.0)	12 (20.7)

Employment status		
Employed	38 (76.0)	34 (58.6.)
Not employed	10 (20.8)	22 (37.9)
Missing	2 (4.0)	2 (3.4)
Education		
Secondary & A levels	19 (38.0)	28 (48.3)
Degree	12 (24.0)	12 (20.7)
Other/professional	16 (32.0)	15 (25.9)
Missing	3 (6.0)	3 (5.2)
Marital status		
Married/cohabitating	42 (84.0)	48 (82.8)
Single, widowed, divorced	8 (16.0)	10 (17.2)
Lymphoedema		
Yes	23 (46.0)	22 (37.9)
No	27 (54.0)	36 (62.1)
Number of children		
No children	5 (10.0)	7 (12.1)
Children	42 (84.0)	49 (84.5)
Missing	3 (6.0)	2 (3.4)
Using hormone therapy		
Yes	36 (72.0)	43 (74.1)
No	14 (28.0)	15 (25.9)
Treated with chemotherapy		
Yes	39 (68.2)	41 (70.7)
No	11 (31.8)	17 (29.3)
Treated with surgery		
Mastectomy	25 (50.0)	32 (55.2)
Breast conserving surgery	25 (50.0)	26 (44.8)
Treated with radiotherapy		
Yes	41 (82.0)	43 (75.4)
No	9 (18.0)	14 (24.6)
Missing	0	1 (1.7)
Months post treatment	18.4 (16.2-20.6)	16.6 (15.2-18.1)
Length of treatment (months)	7.8 (6.5-9.8)	8.1 (7.0-8.9)

6.8 DISCUSSION

6.8.1 RESPONSE RATES AND ELIGIBILITY

This study found the response rate to clinician invitation letters to be 39% which suggests that many breast cancer patients were interested in becoming physically active and were willing to take part in an exercise research trial. The response rate to clinician invitation was encouraging and similar to previous research involving an eight week exercise and diet intervention pilot study [201] which achieved a recruitment rate of 39.6% by invitation letter. In a comparative study of RCT design, 28.2% of post-treatment breast cancer patients responded to a mailed invitation to take part in a 15 week exercise trial.[110]

Despite a favourable response rate, a greater proportion of patients (61%) who were invited by their oncologist or surgeon to take part in the study did not respond or were not further reachable by the research team after the patient had made initial contact. There may be a number of reasons why women declined to take up the offer to get involved in the study, it is possible that these women were already engaging in regular physical activity and therefore would not have been eligible to take part in the study. Based on the number of responders excluded as being too active to benefit from the intervention (n=28) this does seem plausible for some women; although studies have consistently shown that physical activity levels decline significantly after breast cancer diagnosis (82,83) and can remain low for many years after treatment is completed.[76] Other reasons for not responding to clinician invitation may have included fears about exercising after a cancer diagnosis; women may be fearful of over-doing it, and uncertain about their abilities to be physically active.[202] It has been reported that patients are sometimes reluctant to participate in RCT's because they do not want to be allocated to a no treatment arm.[203] Additionally, some women

may have been reluctant to take up the opportunity to get involved in an exercise based study because they may be unaware of the potential benefit of exercise therapy for breast cancer patients. Patients are offered limited advice regarding what is considered to be appropriate exercise post treatment [69] and may have held the impression that *'rest is best'*, preferring to conserve energy rather than expend it participating in an exercise programme. Research by Wright et al [204] found that cancer patient's perception of gaining personal benefit was the most important predictor of their decision to enter an RCT.

Future trials might benefit from designing recruitment strategies that better address both the potential benefits of exercise participation and the concerns that breast cancer patients might have about engaging in exercise. This type of strategy that focuses on some of the motivators and barriers to participation in trial recruitment literature was used successfully by Ott et al [198] who recruited breast cancer patients to an exercised-based intervention for osteoporosis prevention. Alternatively, providing a point of contact for women to talk to a health professional about their concerns and anxieties as they relate to exercise might also help with recruitment to such trials. For these reasons it could be that approaching patients during follow-up hospital clinic visits would result in higher recruitment figures than by clinician invitation letters because patients' fears about exercise could be addressed directly by health professionals during appointments. However this approach would prove much more time consuming and costly, relative to clinician invitation letters.

6.8.2 RESPONDERS AND NON-RESPONDERS

It was initially expected that it might be more difficult to recruit older and less affluent women into an exercise trial. Recruitment findings from Project Lead, [197] a lifestyle-based exercise and diet intervention for older (65 years or more), newly

diagnosed prostate and breast cancer patients found that respondents, compared to non-respondents, were significantly younger, were less months post-diagnosis and more likely to be white and male. The authors of the Project Lead study also reported that 54% of responders to mailed trial invitations were already engaging in exercise and 11% were following a healthy diet, leading to the conclusion that recruitment strategies may have yielded a biased sample. Situational barriers such as transport problems and conflicts with work were cited as two of the three main reasons as to why 697/1144 women being treated for breast cancer declined to attend a pre-screening assessment for an exercise based RCT in the UK.[205] This evidence suggests the need for researchers to try and address these types of barriers in the design of future exercise intervention studies.

Results from this study suggest that level of deprivation may influence breast cancer patients' decisions to enter a RCT of exercise therapy; this is in broad agreement with evidence that has reported low socio-economic status is inversely associated with clinical trial participation.[206] Therefore, researchers should aim to make trial participation a financially viable option for all. This may mean subsidising travel or finding new ways to bring reach all participants, or by offering home-based interventions.

6.8.3 RECRUITMENT RATE

The estimated trial recruitment rate of 28.6% of eligible patients recruited by clinician invitation was affected by strict eligibility criteria in this trial. Most notably, many potential patients were excluded because they were too active. While contributing to recruitment challenges, this restriction allowed for the assessment of the impact of exercise on trial outcomes in women who were not already benefiting from exercise.

Relatively few exercise RCT's with cancer patients have reported their recruitment rates but of those that have, less than 40% of eligible patients are typically recruited.[110,114,128,197] An exercise trial involving a mixed population of cancer patients [127] was able to recruit 80% of eligible patients although a control arm was not included. A very high recruitment rate (94%) was recorded in a recent trial [207] conducted in Canada of the effects of an oncologist's recommendation to exercise in newly diagnosed breast cancer patients upon self-reported physical activity over five weeks from baseline. This study however, did not require patients to attend an exercise facility over several weeks or be willing to commit to being physically active over the intervention period. Recent research has revealed some of the important factors that may help to facilitate recruitment arising from the cancer patient and research team interaction. Wright et al [204] found that perceived time spent with the patient, impartial support from the research team to help patients make their decision and physician endorsement were all significantly ($p<0.05$) correlated with a patients decision to enter a clinical trial. This evidence lends support for utilising clinically based (if necessary), trained trial recruiters who can communicate with empathy and help patients with their concerns about taking part in an exercise based trial. It is also imperative that recruiters can provide patients with sufficient information and clarity to allow them to make decisions regarding informed consent. [203] The method of employing clinical recruiters was successfully undertaken in a recent UK based study, whereby 80% of eligible patients undergoing treatment were approached by clinically based trial recruiters.[205]

6.8.4 ROUTE OF RECRUITMENT, DEMOGRAPHIC AND HEALTH BEHAVIOURS

In this study randomised patients recruited from different recruitment strategies did not vary significantly in terms of their socio-economic status, lifestyle behaviours, type of cancer treatment and treatment side effects. This is reassuring since it suggests that any subsequent trial effects are unlikely to be influenced by the possibility that more motivated (and possibly healthier) women recruited via the community strategies responded differentially to those recruited via clinician invitation letter. Women who were randomised were comparable across the different categories of deprivation. Financial concerns may be a barrier to trial participation for some women, to minimise the likelihood of this being the case all women randomised to the study were reimbursed for travel expenses up to a value of £2.50 per visit. This may have helped to encourage a higher number of less affluent women to take part than would have been the case otherwise.

6.9 STRENGTHS AND WEAKNESSES

This study has several methodological weaknesses that should be considered when interpreting the findings and planning future research. This trial was only concerned with recruiting women aged up to 65 years; therefore the recruitment data may not be applicable to older women who have been treated for breast cancer. An important consideration not addressed in this study was the relative cost(s) of the different recruitment strategies, an evaluation of these costs would have proved useful to help fully determine their effectiveness. The estimated recruitment rate of 28.6% in response to the clinician invitation may be underestimated as all recruitment strategies were running at the same time and therefore some eligible women may have been made aware of the trial via one of the community routes prior to the date by which

they would have been sent their clinician invitation and/or become eligible. Thus, it is possible such women would also have agreed to enter the trial on receiving their clinician letter of invitation, had they received this first.

The examination of the differences between responders and non-responders to clinician invitation was limited to age and level of deprivation. It would have been a useful strategy to request from all the women who were sent a clinician invitation to return (stamped addressed envelope) a ready-made reply slip to indicate reasons for not taking part in the study. This would have provided a more detailed overview of why some women choose not to take part when given the opportunity to do so.

The socio-economic characteristics of women who enquired about the study via the community strategies route but who were ineligible were not systematically logged. Similarly this information would have been useful and future studies should allow sufficient financial resources to gather this type of information.

This study required women in both of the exercise intervention groups to attend three exercise sessions per week for eight weeks. This time commitment may have introduced an element of selection bias, indeed 2.6% of eligible women felt they could not commit themselves to the study due to the perceived time burden, thus the time intensive supervised nature of the exercise intervention may have influenced recruitment.

A very low proportion of black and ethnic minority women were recruited in to this study. Previous exercise trials [110,127] have also recruited very small samples of Black and ethnic minority women. Future studies could target minority populations by engaging community advocates/leaders from within ethnic minority communities. The production of trial adverts (and possibly clinician invitation letters where patients' ethnicity is known) in languages other than English might also prove useful. To ensure

that fears about contact with men during exercise trials does not become a barrier to recruitment for women affiliated with particular religions/cultures, trial coordinators need to consider making female exercise instructors/leaders available at all times, and this information made explicitly clear in trial recruitment literature.

A particular strength of this study is that the relative merits of a range of recruitment strategies were assessed, which previous trials have failed to report. Additionally, unique evidence about the associations between methods of recruitment of breast cancer patients randomised into an exercise trial and their characteristics, lifestyle behaviours and treatment regimens and side effects has been provided, which previously has been an understudied area of research.

6.10 CONCLUSIONS

In summary, both clinician invitation letters and the community strategies contributed substantially to the recruitment process. It does seem that affluent women treated for breast cancer are more likely to respond to the invitation from their oncologist/surgeon than their less affluent counterparts. Patients randomised into the study via different recruitment strategies did not differ significantly in their socio-economic status, lifestyle behaviours, type of cancer treatment or treatment side effects. The trial recruitment rate was generally acceptable, yet likely to be a conservative estimate. Important information was identified that will be valuable for planning recruitment of future exercise intervention trials involving breast cancer patients. Recruitment to this study was an on-going challenge that required careful monitoring. As recruitment was slower than had been anticipated more information is needed to understand the determinants of breast cancer patient's decisions to enter exercise-based clinical trials in the UK. Researchers may want to focus their attention upon reaching all potentially eligible participants and work towards maximising the

response and recruitment rates from various recruitment strategies, including those that were not assessed here.

CHAPTER 7. INTERVENTION ADHERENCE

7.1 INTRODUCTION

There is a growing body of evidence to suggest that breast cancer patients may benefit from structured, exercise therapy based interventions, [102,104] in terms of the attenuation of treatment related symptoms and restoration of physical function and psychological well-being.[109] This type of approach to treatment and rehabilitation management is gaining acceptance as an important intervention both during and post cancer treatment.[208] However, the benefits of exercise are likely only to be achieved through sustained exercise participation.[17,76] This requirement presents a challenge to practitioners and researchers as exercise participation amongst breast cancer patients has been reported to decline during cancer treatment and has been shown not to recover to pre-diagnosis levels.[72,82,83]

7.1.2 ADHERENCE RESEARCH

Researchers have employed randomised controlled design methodology to investigate the efficacy of exercise-based interventions in various cancer populations.[126,128,180,209] However, very few trials have subsequently provided detailed information regarding patients' adherence to the exercise intervention arm(s) of the trial. The identification of the dose of the intervention and how well it is adhered to, is fundamental to defining the utility of the intervention in providing patient benefit relative to the trial outcomes. Most previous studies simply report an overall adherence rate based upon the average adherence achieved across all participants in the exercise intervention arm.[110,114,136,210] Very few trials have provided more detailed information on patterns of intervention adherence such as the duration, intensity and frequency of exercise achieved by patients.

Studies have often failed to report the number of participants who actually achieve the exercise intervention goal. Irwin et al [211] acknowledge the prospect of drawing misleading conclusions from overall adherence rates; in their 12 month moderate intensity exercise study for post-menopausal women, the overall adherence rate to achieving the exercise protocol five days a week was high at 78%, however, closer examination of the adherence data revealed that only 21% of participants achieved the exercise prescription for the intervention over the 12 months. This type of deeper insight is especially important for researchers and clinicians who need to be able to design and offer exercise interventions of a nature that will have a reasonable probability of being adhered to, and thus have the potential to offer clinical benefit.

7.1.3 PRACTICAL CHALLENGES TO ADHERENCE

Challenges to the delivery of exercise interventions and adherence problems have been experienced by researchers in this field; for example Pickett et al [212] found that a third of newly diagnosed breast cancer patients who were allocated to a home-based walking intervention did not adhere to the prescribed exercise protocol, 22% of the women never actually got started on the walking programme and a further 13% did not complete the intervention, ceasing their participation at least one month before the intervention was due to finish. Further, adherence difficulties were encountered by Damush and colleagues [213] who had to modify their original (exercise-based) programme delivery from a group-based intervention to individual sessions and a mailed format to accommodate the varying attendance preferences and needs of the participants. Provision of this type of data is important to help understand the type of intervention and the kinds of setting that will be most preferable and manageable for women recovering from breast cancer.

7.1.4 THE IMPACT OF POOR TRIAL ADHERENCE

Low levels of adherence can lead to a diffusion of treatment, therefore compromising the internal validity of trials. Moreover, if high levels of adherence are not achieved and a non-significant effect is reported between treatment and comparison groups, it is difficult to know whether the non-significant effect is due to the poor adherence within the study, or to an ineffective intervention. Previous exercise trials in the field of oncology have included home-based unsupervised exercise interventions whereby patients have been required to either self-report the amount of exercise they completed each week by completing physical activity logs or report their compliance to the exercise intervention by telephone recall.[116,118,131,207,212] Although these types of studies are of a pragmatic nature and demand less financial resources than facility-based interventions, their assessment of exercise adherence may be subject to issues of bias.

Supervised RCT exercise studies with cancer patients have reported average exercise adherence rates in the range of 60-85%.[114,127,128,162,194,210] In comparison a review of 21 exercise-based RCT's in older adults (aged 55years and over) without cancer reported an average adherence rate between 63% and 88% (of those studies that included drop-outs the rate was 63%).[214] Furthermore exercise adherence was found to be greater in the strength and flexibility type interventions (87%) than in the aerobic exercise interventions (75%).

7.1.5 DETERMINANTS OF PATIENT ADHERENCE IN EXERCISE AND CANCER TRIALS

Cancer patients are required to endure intensive treatment regimes often over a period of several months; it therefore seems plausible that some patients may be more capable of adhering to an exercise intervention than others. In theory disparities in

exercise adherence levels may be due to the different types of surgical and adjuvant treatment received. Following on, the presence of breast cancer related conditions such as lymphoedema may act as a pre-disposing influence on exercise adherence. This information has not been documented by previous reports, therefore it is difficult to know which breast cancer patients are likely to be at risk of drop-out from exercise programmes and require additional support to change their exercise behaviour patterns.

Determinants of higher adherence may be related to patients' socio-economic status and current health behaviours; reviews on physical activity interventions in healthy populations would support this suggestion and have identified advanced age, gender, low educational level, smoking, being overweight and low social support as determinants of poor intervention session attendance.[215] Some recent studies have explored psychosocial determinants of exercise adherence in colorectal [216-218] and breast cancer patients [136,137,169] which collectively found intention and perceived behavioural control to be significant predictors of exercise programme attendance.

Adherence to exercise has been demonstrated to be a difficult challenge for healthy populations, [219] and is likely to be equally, if not more difficult, for patients who have completed treatment for cancer. This notion is substantiated by Courneya and colleagues [136] who caution that adherence rates to interventions that require "physically untrained" breast cancer patients to exercise more than twice a week may be lower than the modest 66% adherence average experienced reported by a trained group of breast cancer patients. Understanding some of the determinants of exercise after treatment for cancer is one of the key strategies towards developing effective interventions.

This study seeks to provide descriptive data regarding the exercise adherence of women allocated to the exercise interventions. The dose of exercise in terms of duration, rating of perceived exertion (RPE) and heart rate (HR), over the course of the interventions is presented. In addition, this study explores differences in intervention session adherence according to patients' route of trial recruitment, socio-economic characteristics, health behaviours, cancer treatment regimens(s) and side effects from treatment.

7.2 METHODS

7.2.1 EXERCISE THERAPY INTERVENTION

Exercise therapy sessions took place on a 'one-to-one' basis with an experienced exercise research assistant and sessions lasted 50 minutes. In line with previously published guidelines for cancer patients [24] the goal of the exercise therapy intervention was to accumulate 30 minutes of moderate intensity (60-85% heart-rate adjusted maximum) aerobic exercise, three times per week over a duration of eight weeks. Participants were encouraged to focus firstly on the frequency of their exercise, and then to focus on the duration and intensity of their exercise sessions. The exercise therapy intervention was guided by a framework (See Figure 7.1) which offered a structured approach to aerobic exercise progression in terms of intensity and duration. Participants were offered a range of aerobic exercise activities (e.g. stepping, cycling, walking, rowing and jogging) in a dedicated private exercise facility. HR and RPE (using the Borg [179] (6-20 scale) were recorded every two minutes during every exercise therapy session; the trial research assistant/exercise therapist documented this information in activity logs. (See chapter 3 for more detailed methods).

Figure 7.1 Exercise therapy intervention framework

	Weeks 1 and 2	Weeks 3 and 4	Weeks 5 and 6	Weeks 7 and 8
Intensity (% age adjusted HR maximum)	60-75	60-75	75-85	75-85
Duration (minutes)	10-20	15-20	15-20	20-30
Frequency (times per week)	3	3	3	3
Type	Aerobic	Aerobic	Aerobic	Aerobic

Note: Exercise therapy sessions lasted a total of 50 minutes and included a five-minute warm-up and cool down and exercise behaviour change counselling discussions.

7.2.2 EXERCISE-PLACEBO INTERVENTION

The exercise-placebo group also attended the trial centre three times per week over eight weeks and participated in 'one-to-one' 50-minute sessions. However, in contrast to the exercise therapy group, in the placebo-exercise group every effort was made to keep HR less than approximately 100 beats per minute so as to limit the aerobic stimulus provided by the intervention and it was intended to keep maintained below 12 (light intensity exercise). HR and RPE were recorded in activity logs for every session. HR and RPE were assessed every five minutes during these sessions. (See chapter 3 for more detailed methods)

7.2.3 USUAL CARE

The usual care group were encouraged to continue with their lives as normal and were offered the opportunity of taking part in three to five exercise sessions at the trial centre after completing their 24-week follow-up assessment.

7.4 MEASURES

At baseline all participants provided information concerning their medical history specific to their cancer diagnosis, use and type of hormonal therapies, type(s) and length of cancer treatment, presence of lymphoedema, stage of disease and time since treatment. Exercise behaviour including frequency of exercise [171,172] per week/month, stage of change for exercise (SOC), [134] BMI, percentage body fat (bioelectrical impedance) and aerobic fitness were also assessed at baseline. Aerobic fitness was measured using a sub-maximal eight-minute single stage-walking test [178] performed on a treadmill. The Index of Multiple Deprivation [181] (IMD) rank score was calculated for each participant based on residential postcode. (See Chapter 3 for more detailed methods).

Adherence was defined as the level of session participation achieved by participants. The dose (in terms of duration, RPE and HR) of exercise achieved by participants during each session was calculated by averaging the data taken from the weekly physical activity logs for each session.

7.5 ANALYSES

Adherence rates were calculated including all women randomised to both interventions irrespective of individual level of compliance. Mean session adherence was calculated for both intervention groups. This was because both the exercise therapy and exercise-placebo interventions involved women making the same effort to attend supervised sessions at the trial centre, and as such both groups of participants were included in the determinants of session adherence analyses. The relationships between route of recruitment and participant characteristics and session adherence were examined using independent t-tests, analysis of variance or chi-squared analysis, depending on the type of data. Participants were dichotomised or categorised according to their particular characteristics and these were used as the independent variables in the session adherence analyses.

7.6 RESULTS

7.6.1 PARTICIPANTS AND DEMOGRAPHICS

A total of 108 eligible patients consented to participate into the trial and were randomised to either aerobic exercise therapy (n=34), exercise-placebo (n=36) or usual care (n=38). The sample size was deemed sufficient to estimate the prevalence of adherence (50% or less) with 10% precision (95% confidence interval).

7.6.2 DETERMINANTS OF SESSION ADHERENCE TO THE TRIAL INTERVENTIONS

There were no significant differences ($p<0.01$) between route of recruitment, socio-economic characteristics, health behaviours, type of treatment regimen or treatment side effects and mean session adherence to the interventions. (Refer to Table 7.1)

7.6.3 SESSION ADHERENCE AND DOSE OF EXERCISE ACHIEVED

Information for HR, RPE and duration of exercise for the aerobic exercise therapy and exercise placebo groups is provided in Table 7.2 and Table 7.3 respectively. Additionally, the percentage of women achieving ≤ 20 min, ≥ 20, ≤ 29 min or >30 min of exercise therapy across the intervention period is detailed in Table 7.2. Adherence to the interventions was acceptable; 77% of the exercise therapy and 88.9% of the exercise-placebo groups respectively attended 70% (at least 17/24 sessions) or more of the prescribed exercise sessions.

7.6.4 EXERCISE DOSE

Over the course of the exercise therapy intervention, the number of participants able to achieve the recommended 30 minutes of moderate physical activity per session increased, (range: 26.5%-52.9%). Table 7.2 describes the amount of exercise, both in terms of intensity (HR and RPE) and the duration of exercise achieved by exercise therapy participants over the eight-week intervention. Variable patterns of adherence were evident over the course of the eight weeks; non-attendance was highest during weeks 7 and 8. A similar pattern of variable adherence was seen in the exercise-placebo intervention. This group also recorded less attendance in weeks 7 and 8. The overall mean percentage of maximum heart-rate achieved during the exercise therapy sessions was 70.7%. During week one the mean percentage of

maximum heart-rate achieved by the exercise therapy participants was 68.3% (7.3 SD) rising to 71.3% (5.6 SD) in week 8.

Table 7.1 Mean session adherence to the trial interventions according to recruitment route and selected baseline socio-economic, lifestyle and treatment regimen outcomes

Demographics	Mean (se)[1] session adherence (range=1-24)[2]
Route of recruitment into trial	
Oncologist letter (n=28)	19.9 (0.50)
Community advertisements[3] (n=42)	19.0 (0.99)
Age, years	
30-49 (n=32)	20.0 (0.56)
50-65 (n=38)	19.2 (0.78)
BMI	
Under/normal weight (n=17)	21.1 (0.59)
Overweight/Obese (n=53)	19.0 (0.61)
Smoking status	
Smoker (n=5)	21.4 (0.68)
Non-smoker (n=65)	19.4 (0.52)
Stage of change for exercise	
Precontemplation and contemplation (n=34)	20.4 (0.51)
Preparation (n=36)	18.8 (0.81)
Frequency of physical activity	
Never (n=18)	20.2 (0.74)
≤3 times per month (n=19)	19.8 (0.76)
Once per week (=20)	17.9 (1.27)
≥Twice per week (n=13)	19.5 (0.87)
Index of multiple deprivation	
Quartile 1 (n=20) (least deprived)	20.1 (0.70)
Quartile 2 (n=19)	19.2 (0.92)
Quartile 3 (n=17)	20.2 (0.85)
Quartile 4 (n=13) (most deprived)	18.4 (1.73)
Missing (n=1)	
Treated with chemotherapy	
Yes (n=52)	19.7 (0.87)
No (n=18)	19.5 (0.60)

Treated with surgery	
Mastectomy (n=36)	19.1 (0.79)
Lumpectomy (n=34)	20.1 (0.57)
Treated with radiotherapy	
Yes (n=55)	20.2 (0.70)
No (n=15)	19.4 (0.60)
Lymphoedema	
Yes (n=27)	19.7 (0.71)
No (n=43)	19.5 (0.70)

[1]Refers to standard error.

[2]Includes both intervention groups.

[3]For analysis purposes the recruitment routes of cancer care support groups, breast cancer nurses, media advertisements and word of mouth were combined into a single route of recruitment referred to as community advertisements.

Table 7.2 Adherence to the exercise therapy intervention

Exercise therapy (n=34)	sessions							
	1-3 (Week 1)	4-6 (Week 2)	7-9 (Week 3)	10-12 (Week 4)	13-15 (Week 5)	16-18 (Week 6)	19-21 (Week 7)	22-24 (Week 8)
HR (Mean, SD)[a]	115.6 (12.9)	119.2 (12.9)	118.8 (12.8)	118.5(12.6)	119.7 (15.4)	123.3 (11.3)	121.6 (12.3)	121.2 (11.0)
RPE (Mean, SD)	11.1 (1.2)	11.8 (2.2)	11.5 (1.4)	11.1 (1.4)	11.4 (1.2)	11.3 (1.2)	11.4 (1.2)	11.4 (1.0)
Duration of session mins (Mean, SD)[a,,b]	24.1 (6.5)	27.2 (6.0)	27.3 (5.9)	26.2 (6.3)	27.4 (6.0)	27.3 (6.3)	27.5 (6.2)	26.9 (6.8)
	Session 3	Session 6	Session 9	Session 12	Session 15	Session 18	Session 21	Session 24
Percentage achieving[c]								
≤20min	5.8	2.9	0	0	0	2.9	0	0
≥20-29min	35.4	32.3	32.3	38.2	26.4	17.5	11.7	17.7
30min	26.5	41.3	29.4	29.4	52.9	44.1	47.2	29.4
Did not attend[c]	32.3	23.5	37.9	32.3	20.5	35.3	41.4	50.0

[a] Data is based on aggregated scores from sessions across each week.
[b] All aerobic exercise sessions lasted a total of 50min. Sessions included a warm up and cool down as well as discussions about exercise behaviour change strategies.
[c] Percentages are based on the number of women who attended or did not attend the final exercise therapy session each week (i.e. sessions 3, 6, 9, 12, 15, 18, 21 & 24).

Table 7.3 Adherence to the exercise-placebo intervention

Exercise-placebo (N=36)	sessions							
	1-3 (Week 1)	4-6 (Week 2)	7-9 (Week 3)	10-12 (Week 4)	13-15 (Week 5)	16-18 (Week 6)	19-21 (Week 7)	22-24 (Week 8)
HR (Mean, SD)[a]	92.3 (10.7)	93.8 (9.8)	95.0 (9.8)	96.8 (9.1)	94.1 (9.6)	94.2 (9.2)	93.3 (12.4)	91.7 (13.9)
RPE (Mean, SD)[b]	10.7. (1.2)	10.9 (1.1)	10.9 (1.2)	10.9 (1.3)	10.7 (1.4)	10.8 (1.7)	10.5 (1.4)	10.5 (1.6)
	Session 3	Session 6	Session 9	Session 12	Session 15	Session 18	Session 21	Session 24
Percentage who did not attend[c]	0	0	2.7	0	5.7	14.2	44.4	72.2

[a] All placebo sessions lasted 50 minutes.
[b] Data is based on aggregated scores from these sessions across each week
[c] Percentages are based on the number of women who did not attend final exercise placebo session each week (i.e. sessions 3, 6, 9, 12, 15, 18, 21 & 24

7.7 DISCUSSION

7.7.1 INTERVENTION ADHERENCE

Previous research has suggested that exercise-based randomised controlled trials (RCT) need to be designed to enhance exercise adoption and to facilitate regular attendance. As is the case for all types of behavioural interventions, the benefits of exercise can only be experienced by cancer patients through regular participation. In this study women treated for breast cancer achieved an acceptable level of overall aerobic exercise adherence (77%) and the percentage session adherence rates are comparable with other supervised RCT's with cancer patients.[114,127,128,162,194,210] Moreover, the adherence rate from this study surpassed that observed in other studies involving non-diseased individuals.[214]

7.7.2 PATTERNS OF ADHERENCE

Of those participants who attended the exercise therapy intervention, between 26.5-52.9% were able relatively quickly to adapt to achieving 30 minutes of structured moderate intensity exercise three times per week at the centre for any given week/session (Refer to Table 7.2). This is encouraging as it demonstrates that previously sedentary breast cancer patients provided with access to facilities and supervised support can become more physically active. It also moves patients closer to meeting the current public health recommendation of 30 minutes of moderate intensity exercise on five days of the week.[65]

Previous trials involving cancer patients have typically only reported overall adherence rates to exercise interventions. Understanding the number of participants who adhered to the behavioural goal of the intervention and/or the dose of exercise achieved by participants within sessions and across weeks provides a more meaningful insight. For example, data from this study showed the number of sessions

completed by the aerobic exercise therapy group was high at over 70%, the amount of aerobic exercise achieved steadily increased implying the intervention was tolerated by, and acceptable to, women recovering from breast cancer. However, on further inspection of the adherence data, the proportion of participants in the exercise-therapy group who did not attend sessions increased over time. This trend was also observed in the exercise-placebo group. The trend toward diminishing exercise attendance over time has been observed in other healthy populations [214,219] and may be a reflection of the continuous physical and psychological demands of achieving regular exercise participation. Given this to be the case it highlights the need for researchers and clinicians to monitor participant adherence and intervene with practical strategies to support participant's behaviour change wherever possible.

Reasons for non attendance were not systematically recorded in this study, but participants who took part also had commitments such as work, family and child care responsibilities. Recent research substantiates this potential interruption to exercise attendance as Courneya et al [170] reported that breast cancer patients were less confident they would exercise if they experienced family responsibilities. It is also possible that in the current study exercise attendance was interrupted by holidays and illness.

Common exercise adherence barriers in cancer populations have been reported to include inconvenient exercise schedules, lack of time, perception of exercise as being boring and financial costs of travel and parking.[220-222] This study aimed to facilitate participants' visits to the centre by offering participants the opportunity to exercise at various times of the day, including evenings and weekends, providing parking facilities and by offering a variety of exercise equipment and stimulating exercise programmes.

The progressive intensity dose of exercise achieved by participants was in line with the trial protocol with participants on average exercising at moderate-hard intensity throughout the intervention. However, there appears to be a small discrepancy between HR and RPE data, in that the HR data indicated participants were exercising at moderate-hard intensity (in accordance with the protocol), whereas RPE data suggests participants perceived they were exercising at light-moderate intensity exercise. As is usual in exercise studies, HR was used as the primary regulator of exercise intensity but the data does nevertheless highlight an important issue in the regulation of exercise intensity in cancer patients and the need to adopt both an objective and subjective measure of intensity.

It is imperative that participants appreciate the difference between the measures of RPE and HR and are able to safely regulate their exercise efforts so as to avoid over-exertion. There have been calls for RCT's to include attention-control arms [95,104] where there is considerable patient-practitioner interaction. No previous trial has attempted to randomise breast cancer patients to an 'exercise' based placebo condition. It is only reasonable and responsible of researchers to offer meaningful placebo interventions given that participants will be investing considerable time in taking part in a trial. Participants are unlikely to adhere to a meaningless placebo intervention that demands their time. Exercise-placebo conditions have additional complications because patients cannot be blinded to group assignment. Like any trial that includes a placebo arm, it is possible that participants become aware that they are not receiving an 'active' treatment or they become demoralised that they did not receive the 'alternative' treatment that may have been on offer. The session adherence rates to the exercise placebo intervention suggest this study provided an authentic alternative to the exercise therapy intervention; indeed, session adherence was

marginally higher for the exercise-placebo than for the exercise therapy intervention group.

Table 7.3 confirms that the HR of the exercise-placebo group, on average, remained less than 100 beats per minute as per the intervention protocol. Furthermore, typical average RPE scores across the intervention period ranged from 10-11; this is considered to be within the low intensity exercise range, further substantiating the minimal aerobic content of the exercise-placebo intervention. Nevertheless, RPE scores in the exercise-placebo were higher than expected; particularly given that participants' corresponding HR scores were within the low intensity range. Recent propositions [223,224] have suggested that chemotherapeutic treatment may be responsible for neurotoxicity and myotoxicity which would affect muscular function and flexibility in particular.

7.7.3 DETERMINANTS OF EXERCISE SESSION ADHERENCE

The apparently high overall session adherence rates, coupled with the lack of any significant findings in the determinants of session adherence analyses suggests that women treated for breast cancer are keen to participate in exercise intervention programmes when given the opportunity and support to do so. The findings from this study are in contrast to others; predictors of exercise adherence in colorectal cancer patients included SOC for exercise, employment status and treatment protocol, [218] in prostate cancer patients SOC for exercise, age and intention were all independent predictors of adherence.[225] This study focused its attention on understanding the socio-demographic, health behaviour and treatment factors as likely determinants of exercise behaviour. Alternatively investigation of psycho-social determinants of exercise adherence may reveal a greater influence than those factors evaluated in this study. Indeed several studies [135,136,169,170,191] have found associations between social

cognitive variables (e.g. attitudes, perceptions of control, intentions, subjective norms, self-efficacy) and health behaviours in breast cancer patients, but these studies were conducted in other countries and as such their findings may not transfer to this setting.

7.8 LIMITATIONS AND STRENGTHS

The sample recruited in this study was relatively homogenous in respect of their health behaviour and treatment variables; therefore the findings of this study may not be transferable to other breast cancer patients who demonstrate more diversity. Furthermore, participants were predominately of White ethnic origin and therefore our findings should be generalised to women of other ethnicities treated for breast cancer with some caution. The sample size is relatively modest and larger studies may be better able to provide more precise estimates regarding the determinants of exercise adherence in this population. The supervised nature of both interventions meant it was possible to systematically record HR and RPE, as well as the duration of exercise; this provided the opportunity to examine in detail the precise intensity and dose of exercise achieved by participants during the interventions and this is an important strength over previous trials.

7.9 CONCLUSIONS

Examining the efficacy of an intervention crucially requires adequate adherence. The findings demonstrate that there was favourable session adherence indicating that in the context of an RCT a supervised aerobic exercise therapy intervention was acceptable to women treated for breast cancer. Further research is needed to identify all the potential determinants of exercise in this population. Designing interventions to enhance regular exercise remains a challenging proposition. Exercise adherence is an ongoing challenge for both patients and practitioners.

CHAPTER 8. QUALITATIVE INVESTIGATION

8.1 INTRODUCTION

There is increasing support for combining qualitative and quantitative approaches to health service research [226,227] to facilitate a more comprehensive, reflexive analysis of the data.[228,229] The rationale for conducting a qualitative investigation after completion of the eight week exercise intervention was to triangulate and furnish the inferences drawn from the quantitative findings (Chapter 4). The quantitative approach undertaken in this study, thus far has aimed to measure the impact of exercise rehabilitation upon breast cancer patients quality of life (QoL) and associated well-being. Adopting a qualitative approach will hopefully generate an understanding of the processes by which exercise rehabilitation may influence QoL and well-being. It is important to frame the presence and magnitude of any exercise intervention effects within the participants own personal context. By obtaining detailed, information data based upon participants' interpretation of their exercise experiences, researchers are better able to understand the meaningfulness of any benefits received. This type of qualitative approach also yields important information for researchers when designing and planning future studies, for example participants can communicate their exercise programming preferences and highlight any barriers they perceive will get in the way of their exercise participation. Taking this information on board, researchers can design suitably tailored interventions that may help to maximise trial adherence.

8.1.2 QUALITATIVE EXERCISE AND CANCER STUDIES

There have been a limited number of studies that have utilised a qualitative methodology to explore cancer patients experiences relating to exercise participation.[170,221,222,230-235] A feasibility study of a 10-week exercise-based rehabilitation programme in the U.K., by Stevinson and colleagues [222] used semi-

structured interview methodology to ascertain patients' perceptions of the programmes acceptability and tolerability. Positive features of the exercise programme were identified and the role of exercise in promoting recovery was revealed through the qualitative investigation. The same methodology was adopted by Hennessy and colleagues [231] in a pilot study to explore the experiences of female cancer patients who had taken part in Race For Life (Cancer Research UK charitable event), conversations revealed how being involved in the event had proved to be a positive focus for the women after their cancer treatment. In Scotland, an evaluation of a group-based exercise programme for breast cancer patients during treatment, by Emslie et al [230] used focus group methodology to explore the factors that influenced exercise programme adherence. Through the group interaction and free expression of the participants exercise experiences, researchers were able to learn that the programme was perceived as being preferable to a conventional cancer support group intervention and that the group format of the exercise programme was perceived to be of great value.

8.1.3 AIM OF THE QUALITATIVE INVESTIGATION

This study aimed to gain an insight into the personal experiences of participants who had taken part in the exercise interventions.

The objectives were to;

1) To understand participants' exercise perceptions and experiences pre-cancer diagnosis.

2) To understand the impact of participant's cancer diagnosis and treatment upon their subsequent exercise perceptions and intentions to participate in exercise (prior to entering the current study).

3) To explore participant's experiences of taking part in the exercise sessions in the current study and the perceived benefits accrued from their exercise participation in the current study.

8.2 METHODS

The current study was a three arm RCT (Refer to Chapter 3 for detailed methods). Participants were randomised to one of three groups: supervised exercise therapy, exercise-placebo (attention–control) or a usual care group as described in Chapter 3.

In this qualitative study the exercise experiences of both the exercise therapy and exercise–placebo participants were investigated. Participants from both exercise arms of the trial were included in this qualitative investigation as both groups of participants had to make the same level of commitment and effort to attend the exercise sessions at the trial centre. Both groups of women engaged in an exercise intervention, albeit differing in exercise modality and intensity. Ethical approval for this study was obtained from the South Sheffield Research Ethics Committee (Reference number 02/226).

8.2.1 PARTICIPANTS AND INTERVIEWS

A purposive sampling strategy [236] was used to create an interview sample. A strategy of interviewing participants with a range of scores (from baseline) on the Functional Assessment of Cancer Therapy– Breast (FACT-B) scale was used. This strategy was undertaken with the intention of exploring the experiences of participants who had different perceptions of their breast cancer -specific QoL. All participants approached to take part in an interview accepted the invitation.

8.2.2 THE INTERVIEW SCHEDULE

An "a priori" semi-structured schedule (see Appendix 16) was used to structure and guide the line of questioning in the interview. Flexibility within the interview schedule allowed the research assistant to accommodate further prompts and probes. Crucially the participant was also able to freely respond to questions and expand upon unanticipated areas of interest and study outcomes. The interview schedule was designed specifically for the present study.

Following background reading and upon reflection of the anecdotal conversations encountered with the participants throughout the intervention period of the study, the interview schedule included mainly open ended questions on the topics outlined in Figure 8.1

Figure 8.1 Interview schedule

- Prior to cancer diagnosis and treatment:

  Exercise history and behaviour, perceptions and attitudes about exercise

- During and upon completion of treatment:

  Exercise behaviour, physical capacity to exercise during and after treatment, perception / attitude toward exercise, intentions and motivation towards exercise

- Your exercise study experiences:

  Reason for taking part, perception of exercise sessions, likes and dislikes, exercise preferences, what benefits were gained from the study? Changes in attitudes, intentions, motivations towards exercise.

- Future intention toward continuing exercise: thoughts on sustaining participation, starting sooner, general comments.

The interviewer was the research assistant who had been in contact with the participants during the exercise intervention and throughout the course of the study. Although this aspect of the methodological approach was not ideal, it was unfortunately dictated by resource constraints. It did however create a sense of ease because the interviewer was already familiar to the participants. The interviewer had previous experience of conducting semi-structured interviews with cancer patients. The first interview was used to test the acceptability of the proposed semi-structured interview schedule and to detect the important themes for questioning and inquiry, acting as a pilot interview. However, it provided a valid response and as such was included in the analysis. No major changes were made to the interview schedule after pilot testing.

The semi–structured interview schedule led to a framework that shaped the data collection, the data generated was largely due to the direction and focus of the questions asked, but the agenda was flexible enough to allow participants to express their experiences in their own way, in whatever order they wished.[237] New ideas that were not anticipated at the beginning of the interview were given time to be explored. The wording and order of the questions was not always scripted as per the schedule, as the researcher tried to frame questions in response to the participant's comments. The researcher aimed to facilitate interaction with participants, but also tried to maintain an objectivity so as to decrease interviewer bias and ensure that the data generated would be only representative of the participant's experiences. Additionally very brief "field notes" were made by the interviewer. These notes constituted brief jottings about the dynamic of the interview, such as non verbal cues like laughing, emotion or the emphasis placed on certain points. All interviews were held in a private room at the university facility which had discrete audio and video taping facilities. These recording methods were used to facilitate transcription of the interview data. Informed consent was given at the start of the study and participants were assured of patient confidentiality. Interviews took place within one week of completing the respective exercise interventions.

8.3 DATA ANALYSIS

Framework analysis [238] was employed in this investigation as this approach defines a systematic process to analyse qualitative data. The method of interviewing generates rich descriptive data, however this requires the researcher to conduct considerable analytical interpretation to identify associations and relationships within the data. This approach to the analysis is somewhat inductive, that is, it is based in the original transcripts of the interviews but framed within the "constraints" of an a-priori

framework.

The audio and video tapes were transcribed verbatim by the study researcher and along with another investigator the transcripts were independently read. The views expressed by participants are those from a post-treatment perspective.

The investigators became familiar with the data by immersing themselves in the verbatim transcripts and field notes, becoming familiar with their content. Meetings were held to agree upon a thematic framework, agreed revisions were made and emergent themes were coded according to the framework. This required intuitive judgements to be made regarding the meaning of the textual data. Analysis was undertaken within the transcripts and between them. The transcripts were searched for similarities and discrepancies within and across the data and were searched for disconfirming cases. An additional investigator (who had not met the participants) verified the thematic framework, indexing and interpretation of data. Through the data analysis it was evident that the participants from both the exercise intervention groups did not differ in terms of their perceived experiences to their exercise sessions. Indeed there were clear commonalities between the groups despite undertaking different exercise modalities. For this reason it was decided not to present data separately for each group, rather to present data from across both groups.

8.4 RESULTS

8.4.1 PARTICIPANTS

In total 12 participants, made up of six exercise therapy (E) and six exercise-placebo (E-P) participants with a mean age of 51.5 years (SD±10.1) took part in the interview study. The mean number of months post-treatment was17.6 (SD± 5.6). All participants were of white ethnicity. Three participants had lymphoedema. (Refer to Table 8.1for treatment regimen characteristics of the sample).

Table 8.1 Interview participant characteristics

Participant	Group	Age	Surgery	Adjuvant treatment	Months post - treatment	Lymphoedema status
1	EX	42	M + recon	CH + HT	12	None
2	E-P	46	M	CH + HT	15	None
3	EX	41	L	CH + RT + HT	24	None
4	EX	64	M	CH	19	None
5	E-P	40	L	CH + RT + HT	16	None
6	EX	39	M + recon	CH	18	None
7	EX	62	M	CH + RT + HT	25	Yes
8	E-P	52	L	CH + RT + HT	12	None
9	E-P	61	M	CH + HT	29	Yes
10	E-P	47	M	CH + RT + HT	12	Yes
11	E-P	63	M	CH + RT	14	None
12	Ex	62	M + recon	HT	16	None

EX - Exercise therapy, E-P – Exercise- placebo, L - Lumpectomy, M - Mastectomy, recon - breast reconstruction, CH - Chemotherapy, RT - Radiotherapy, HT - Hormonal therapy.

8.4.2 THOUGHTS UPON EXERCISE PARTICIPATION PRE-CANCER DIAGNOSIS

Upon reflection the majority of participants considered that any exercise they had taken pre-diagnosis was part of their usual daily routine, (i.e. walking to the shops, gardening, being active looking after the family, being busy at work or making the effort to use the stairs at work). For nearly all women exercise was not a structured, regular activity. Some participants felt that they had been "getting enough" exercise through their usual work /family routine. Common reasons for not taking more exercise were too busy at work and home, thus exercise was not a priority, a struggle to find the motivation to exercise, the perception that exercise (perceived of as gym-based exercise) was not the thing for an older person, that gyms were for sporty, thin types and there was a common misperception that exercise had to be of a vigorous intensity to be beneficial;

> *"I always associated exercise you know that if you did it, it's like no pain no gain"*
>
> (Participant, 2 E-P)

For the few women who had attempted to engage in some form of exercise after completion of their treatment, they reflected that engaging in exercise had been more difficult physically than they expected.

8.4.3 THOUGHTS ABOUT EXERCISE DURING TREATMENT AND AFTER BREAST CANCER TREATMENT

When asked if participants had thought about trying to become more active after their treatment had finished, the consensus was no, due to the side effects of treatment;

> *"Oh no, no way, just tired and exhausted and I was just doing nothing all day and I was still getting tired and the weight was just piling on"*
>
> (Participant 8, E-P)

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>
> (Participant 8, E-P)

"when I finished the chemo I expected to be up and running and all sorts but it doesn't happen like that, you're still feeling tired, again my mind was wanting to go, my legs were really heavy even when I walked ("daughter") up to school"

(Participant 1, Ex)

The lack of structure in the day, the prolonged side effects of treatment and the psychological burden of breast cancer resulted in negative emotional feelings for several women. Repeatedly, women conveyed the feeling that they felt they had simply lost confidence in themselves and the motivation to do things. Reduced range of shoulder motion post-operatively, weight gain as a consequence of treatment, altered physical appearance from surgery and limited stamina for physical exertion were all mentioned as factors that had played their part in lowering physical self-confidence and confidence toward exercising.

8.4.4 CHALLENGES TO REGAINING NORMALITY

Despite the physical and psychological repercussions of diagnosis and treatment there was a unanimous desire amongst women during treatment and upon completion to want to "feel better," "to do something more," "to be active" as evidenced by the fact that they had responded to recruitment literature about the exercise study. There was a sense that something was needed to fill the gap that was left when the medical treatment had ended. Regaining normality was a key aspiration, this was clarified by comments such as "wanting function back, want my body back." However, several women expressed the view that they did not have the motivation to turn their intentions into action and start engaging in regular exercise either during their treatment or once it had finished;

"I'd not exercised for a while, felt lethargic and to actually get motivated to do something was quite difficult"

(Participant 5, E-P)

8.4.5 FEARS ABOUT EXERCISING DURING AND AFTER TREATMENT

Concerns were raised by some women that exercising might induce or exacerbate lymphoedema. Indeed there was a fear that participating in exercise beyond those given post–operatively for regaining shoulder mobility may do harm or damage; as one woman noted;

> *"I was scared to do any exercises actually...anything with my arm I was just scared to do anything with it"*
>
> (Participant 10, E-P)

This feeling of apprehensiveness was heightened for two women after receiving advice from health professionals regarding the development of lymphoedema. The advice to be careful had made the women feel extremely anxious and cautious in their approach and attitude toward exercising and performing daily physical activities;

> *"- you know the health service, they frighten so much around about lymphoedema you think I just can't do this you know, if I do slightly anything wrong I'm going to lose my arm which I look back now and I'm thinking that's a bit ridiculous it's a bit melodramatic, you think about you want to do exercise but you don't feel very confident.... so if you've not like done much exercise before you're not going to suddenly rush out and think oh right I'll do (some exercise)"*
>
> (Participant 2, E-P)

Most women had not received any specific advice regarding exercising post treatment, one participant stressed the point that exercise had never been mentioned or recommended to her by any health professional during her treatment experience which she found surprising. Another woman said she had been encouraged to rest as much as possible which although seemed appropriate on some days, in retrospect she felt she had heeded the advice too strongly; resting too much when it would have been better to try and be more active. For

some women there were more imminent priorities to focus upon other than becoming more physically active, such as returning to paid work, performing in their role as mother, undertaking work in the home, and other priorities at the time took precedence.

8.4.6 REASONS FOR TAKING PART IN THE RESEARCH STUDY?

A key reason for taking part in the study had been the desire to improve their general feeling of physical well-being, a need to improve their physical function "to feel fitter/ better". The anticipation that the study may be of *"benefit to me"* was a key incentive to take part, one woman explained the reasons why she wanted to take part in the study;

> *"I rang up while I think I was in the middle of treatment, because it was those feelings of I want my body back, I want to be able to do things, but I want to sort of do it in a sort of safe way and also erm, cancer treatment is also very odd, because everything happens very quickly and then it stops which is great because obviously you know your well but it kind of leaves a big hole and you just kind of think I just want to do something more"*
>
> (Participant 2, E-P)

For most women, the invitation to participate in the study presented the opportunity and thus the impetus to start exercising, which had been previously difficult to find on their own terms;

> *"Well if I'm honest the main reason was because that I felt like I needed some exercise and I needed a bit of encouragement to go and do it and I felt that if I could get involved with this I would have to do it rather than be left to my own devices and also I felt that if I could help anyone else with this problem then that is what I wanted do"*
>
> (Participant 9, E-P)

8.4.7 PERSONAL APPREHENSIONS AT THE START OF THE EXERCISE SESSIONS

Several women recalled that they had apprehensions prior to engaging in the exercise sessions. These apprehensions were related to concerns that the exercise "may do damage" or exacerbate lymphoedema. Additionally, some women had felt anxious that they would look "daft" or "silly" on fitness equipment that they were not familiar with. The most mentioned apprehension was that women doubted their physical ability to undertake and complete the course of exercise sessions. There was a general concern that the exercise might be "too hard".

8.4.8 FACTORS CONTRIBUTING TO THE ENJOYMENT OF EXERCISE SESSIONS

Overall, the women made very positive comments about taking part in the exercise sessions and there was universal agreement that the sessions had been enjoyable;

"Well, I have enjoyed them and I have been really surprised because I thought it was going to be much harder than it was"

(Participant 11, E-P)

Several women were appreciative of having the opportunity to be involved in the decision making process; choosing which exercise to perform or which piece of equipment to use; this client-centred approach was seen as an important and valuable characteristic of the delivery of the exercise sessions. The enjoyment of exercise sessions was often attributed to several factors in combination such as the satisfaction derived from progressing in one's exercise capacity, the variety of exercises and equipment on offer and the ability to safely exercise without experiencing any pain;

"I felt fitter, although I enjoyed walking it's different when you are doing a different exercise and achieving those goals, on starting to do a bit of jogging on the treadmill and on the rower beating your own time and things you know"

(Participant 3, Ex)

Establishing a regular social routine again was a valued by-product of trial participation, this seemed to be of greater importance for those women who had not yet returned to work or who were socially more isolated living on their own.

"I think I needed a push and this has been that push"

(Participant 3, Ex)

"Doing what I did has motivated me again it has given me a kick start to get back into something"

(Participant 5, E-P)

8.4.9 THE INSTRUCTORS CONTRIBUTION

The exercise instructors were praised for their skills at delivering and managing the exercise sessions. The creation of a relaxed, friendly, non-pressured atmosphere, were reported to help settle women into their new routine and surroundings, in turn the familiarity with the same instructor and the routine of regular, convenient appointment times seemed to foster exercise compliance. Many women made reference to the instructors' ability to be empathetic and encouraging; at the same time the women also approved that the instructors prompted the women to progress (in accordance with intervention allocation). A trusting relationship was created between the women and the instructors, so when the women were asked to exercise harder or to try new things they were not afraid to comply; comfortable in the knowledge that the therapist would not be pushing them beyond their capabilities;

"it was quite relaxed about which equipment I went on and then as I got into other exercises..."therapist"... coaxed me onto the others which I was really anxious about, but glad I went on then because it was like a progression"

(Participant 1, Ex)

Women made reference to the therapist's ability to pitch the exercise at the right level - described as the therapists' awareness and sensitivity to the women's apprehensions and understanding of their lack of exercise experience;

"I felt comfortable, I wasn't made to feel right oh you can't do this, I just enjoyed coming, it was just the routine that I enjoyed and it made me do it"

(Participant 6, Ex)

Women also revealed that, exercising under the guidance of a therapist who understood their condition and breast cancer specific concerns gave them peace of mind that they were exercising in a safe environment, easing nervous apprehensions.

8.4.10 PERCEIVED PHYSICAL BENEFITS

In the course of the interviews all the women commented upon having a tangible feeling of "feeling fitter" and "well" and for most this was referred to as an increased confidence in their physical ability to exercise and increased confidence in their body;

"I feel a bit more confident in myself, although I've not lost weight and I have toned up a bit, I feel a bit more confident with my body than I did before"

(Participant 3, Ex)

"I noticed that my reach and everything had improved under my arm, the stretching had obviously worked....you were exercising but it was quite relaxing exercises really sometimes, so I was surprised really, but I could tell like my bum, my legs felt more toned after doing it"

(Participant 5, E-P)

The concept of feeling fitter was variously interpreted and described as being able to walk further, feel more supple, able to reach farther, having improved posture, for example being "less hunched over", having a more "toned up" body, and generally feeling physically more capable or being able to "do more". Collectively these palpable and

perceptible feelings were put forward as explanations for their new found sense of physical well-being. Furthermore some women went on to remark that after their exercise sessions they had felt energised, even exhilarated, one woman explained how she felt "buzzing" after her exercise sessions. The exercise sessions had not made women feel particularly tired and as one woman remarked she found the exercise intensity very tolerable;

> *"it was not as hard as I thought it was going to be definitely, I found it quite easy really, I never found it strenuous really"*
>
> (Participant 3, Ex)

This reflection contrasts markedly with the difficult self-initiated exercise experiences women had commented upon when they had tried to initiate exercise during treatment and post-treatment by themselves. The impact of exercise upon sleep patterns was surprising; a couple of women shared how they were sleeping better but for others exercise had no subsequent effect on the quality of their night's sleep. It would seem that participation in regular exercise on the one hand did not induce or exacerbate any significant day time fatigue but on the other hand it did not consistently benefit sleep patterns, as the following quotes illustrate;

> *"it was only the first couple of weeks because I felt really tired and thought I don't think I can keep this up, but then I don't know what happens to you - your fitness improves obviously and then I haven't really felt that tired since then, sleeping - I suppose I've been sleeping quite well really, a bit mixed my sleep certainly I haven't been sleeping any less, possibly helped a bit with sleep"*
>
> (Participant 12, Ex)

Although weight gain had been mentioned as a particular concern resulting from treatment and inactivity, for most women exercise participation had provided other benefits equally as important as weight loss;

"it's not just about losing weight, but feeling fitter and better in self".

(Participant 3 Ex)

"Well I've got a new attitude to exercise, a new if you like...in a sense a new outlook on what's important and my blood sugar's have improved and my blood pressure's improved, so that's quite a good pay off isn't it?"

(Participant 7, Ex)

8.4.11 PERCEIVED PSYCHOLOGICAL BENEFITS

Most women had experienced some form of loss of confidence either physical or mental during their diagnosis and treatment experience. The most consistently described psychological benefit of exercise was "increased confidence in self." The sense of achievement in completing the exercise programme and attainment of exercise goals, establishing a new routine, exercising without pain, and being involved in a "non medical context and approach" had all contributed to improved confidence levels that exceeded participants' expectations. Regaining normality, feeling happier and having had the opportunity to try exercise safely succeed and re-evaluate their exercise attitudes allowed for the creation of an optimistic, more positive outlook on life, or a *"different mindset".*

"I don't feel as lethargic I feel more like doing things than I did before and also mentally more positive about the future, I think before I came I did keep thinking that you know I wasn't going to live much longer and things like this",

(Participant 9, E-P)

This woman then went on to offer an explanation of the mechanisms she felt were underpinning the positive change in her outlook;

before I came here I wasn't doing not very much really and I'd got more time to sit and think about it but because now I'm doing this and I feel a bit fitter and I'm actually going out more and doing other things, ...I think I am walking further now and doing more and because of that there are things happening around and you don't think about it (cancer)"

(Participant 9, E-P)

Time since diagnosis and treatment was commented upon as being a potential moderator for positive adjustment, women did in general feel as though the exercise programme had accelerated their recovery, even beyond more conventional therapies on offer;

"it's like before you can't see the woods for the tress, it's all muddled, whereas now I don't think about the cancer as much, I have moved on...and doing the exercises or it's because of the length of time as well, but yeah, you do think about cancer- but it won't take over"

(Participant 1, Ex)

"I did do counselling, I went through a series of counselling sessions erm, but nothing has helped me as much as the exercise in fact it really surprised me to the extent of how I felt afterwards, after the exercises"

(Participant 1, Ex)

From the conservations with the women the impact of exercising upon psychological health was evident. The benefits of the exercise programme had welcomed transferable effects into other areas of the women's lives– notably increasing their capacity to do activities with their families and in the feeling of self-assurance and confidence;

"....Like motivation and things like that, I find I have more energy to do stuff with the children, so yes it's made a big difference"

(Participant 5, E-P)

"not just in exercise but, in, in my outlook on things – do you know what I mean? It's lifted my spirits it sounds weird (laughs) but I feel it's lifted me spirits, not just in doing exercise, but I feel now, I could now take on things that I wouldn't have been able to before, it sounds weird but it's amazing"

(Participant 8, E-P)

Affirmations of their well-being were received from friends and family;

"Well people keep saying how well I look, "you're looking well and you're looking happier", I remember I just used to walk with my shoulders hunched like this (demonstrates in chair, shoulders hunched forwards, eyes looking down) but now I don't, just things like that, just little things that people notice, that I'm a lot happier in myself and that "

(Participant 8, E-P)

The positive shift in health and well-being was echoed by others who felt that by the end of the eight week programme they had made significant progress given their treatment experiences;

"I do feel better, I suppose I feel normal which may not sound a very lot but it's an awful lot from where I've started from"

(Participant 2, E-P)

"so much has changed for me so from when I started at the centre to now, the transformation is huge...it's amazing how the transformation in myself, and I mainly put that down to the exercise giving me confidence, I am more confident, I mean making decisions before I had a problem, so in a positive way I am more confident in the decisions I make and in actually what I do regards myself"

(Participant 1, Ex)

Completing the exercise sessions had empowered some of the women to feel as though they now had the confidence to take on new challenges such as entering Race For Life –

one woman explained how she wouldn't have ever considered herself doing that, expecting it would be beyond her capabilities. For another woman she felt she had now re-discovered the social confidence needed to enable her to start looking for employment again;

> *"it's just given me that motivation to I think right I'm going out Monday, Wednesday, Friday, and I knew exactly what I was doing and it's sort of like a routine which I've not had for over two years you see now, you know if this doesn't help give me a job then nothing will, so it has given me motivation...it has given me confidence because I've been, and got you know, a job"*
>
> (Participant 3, Ex)

On further questioning as to whether it was just a matter of time before her confidence would have returned, the same participant now two years post treatment, elaborated on how the exercise programme had facilitated regaining her confidence;

> *"I think it would have took a lot of time to get...to get that confidence, it would have took a lot longer than eight weeks"*
>
> (Participant 3, Ex)

Exercising under supervision made the women realise that they could exercise without pain and without doing any "damage" to themselves. The women seemed to have valued the opportunity to receive some professional exercise instruction, helping them to understand how to safely perform their respective exercises. This new information had allowed the participants to reshape their old attitudes towards exercise;

> *"I'm more aware of how I should be exercising rather than just going and doing as much as I can, slowing down a bit and doing more, and watching more me heart rate, how I should be exercising"*
>
> (Participant 6, Ex)

"Whereas before I perhaps think I've got to go out and do something more vigorous, but now I've realised you can do more stretching exercises that can make a difference"

(Participant 5, E-P)

8.4.12 THOUGHTS ABOUT FUTURE EXERCISE

The experience and achievement of completing the exercise sessions had fostered a new "can do" attitude toward exercising in the future;

"before I used to think well there's no point me going to a gym because I probably wouldn't be able to manage you know especially with having creaky knees that I've got (laughs) and I used to think I might not be able to do this I might not be able to do that but now that I have been here I think differently I think there's no reason why I can't do it"

(Participant 9, E-P)

"Well it's given me confidence to go on and continue on doing, it's just made me feel a lot better about myself, confidence that I can do it"

(Participant 4, Ex)

The motivations for intending to remain active, primarily included the maintenance of the benefits that had been experienced over the eight weeks of the exercise programme, namely the feelings of being fitter, feeling better, having a routine and the hope that exercise may eventually help with weight loss. There was also a desire not to regress to old ways;

"It's just to keep fit and to be able to run around with the children and be able to go swimming with children, and do things with them rather than thinking I can't do that"

(Participant 6, Ex)

"the fact that I now feel so much better than I did, I can breathe easier and I feel a lot healthier and I want to keep that, and I really want to keep my weight down"

(Participant 9, E-P)

8.4.13 STARTING EXERCISE PROGRAMME SOONER

Several of the women commented that would have liked to have started a structured exercise programme sooner than waiting until being one year post-treatment. There was a general consensus that three to six months after completion of treatment might have been an optimal time to start an exercise programme, it was acknowledged that starting sooner may have proved to be more challenging, so a steady, progressive approach would be preferable.

"I think you could and I think you would get a lot more value, I know it's a bit difficult, it's hard to know but I just think erm, when you finish your treatment you're looking for something and I think in a way that would have helped fill a vacuum and things, it's taken me a like a year for me to think oh, I can do that with my arm, but I'm sure you can do it much sooner"

(Participant 2, E-P)

8.4.14 NON-ENJOYABLE ASPECTS OF THE EXERCISE SESSIONS

The only issues mentioned that affected the enjoyment of the exercise sessions were travelling to the exercise venue and fitting in the commitment of three exercise session a week into an already busy schedule;

> *"the most difficult thing for me is to come from straight from work and then set off to go home and maybe to shop on the way, ...it does make it a bit difficult, I must admit if I had more free time it would have been easier for me... the three times a week, that I found difficult because that's most of your week gone by then"*
>
> (Participant 12, Ex)

> *"no the sessions were fine, it's just what goes with it, getting here with the traffic it's quite time consuming, you know to fit in, even though I'm really flexible"*
>
> (Participant 10, E-P)

8.5 DISCUSSION

This study provided information about the exercise experiences of women who had been treated for breast cancer and who had taken part in a supervised aerobic exercise therapy intervention or a supervised exercise-placebo (light intensity exercise) intervention. The data gathered highlights important information about the participants exercise experiences in the study, particularly with regard to the acceptability of the exercise interventions and the perceived benefits of participating in exercise. These findings may offer direction for future research regarding the planning and implementation of exercise rehabilitation for breast cancer patients.

8.5.1 SOCIAL CONTEXT

Breast cancer treatment had resulted in various physical and psychological side effects that conspired to reduce motivation and physical capacity to become more active and get back to feeling "normal". Loss of confidence both in body and mind, concerns regarding lymphoedema, feelings of fatigue, lack of stamina, reduced arm mobility, lack of routine and the prolonged duration of feeling unwell made women feel emotionally low and lacking the confidence to initiate exercise on a regular basis. Additionally, other priorities such as family and returning to work alongside busy lifestyles and lack of interest in exercise added to the ambivalence around becoming more physically active. It is a well documented observation amongst women treated for breast cancer that exercise levels do not return to pre-diagnosis levels or meet recommended guidelines.[83,87] The treatment and non–treatment related barriers to exercise found in this study are similar to those of other overseas studies. [38,216,221] Hennessy and colleagues (2005) [231] interviewed six post treatment female cancer patients after participating in Race For Life (Cancer Research UK charity exercise event) and found that lack of time and fatigue were main barriers to exercise participation. Survey research by Rogers et al (2007) [220] of breast cancer patients

during treatment lists the top three barriers to exercise as; exercise not being a priority, lack of self-discipline and procrastination (putting off exercise) as reported by 27-52% of the surveyed population. An important observation revealed in the current study is the influence of exercise advice from health-care professionals upon women's intentions to exercise. Minimal or no guidance and over cautious advice had resulted in deterring women from exercise participation. Research undertaken in the United States [88,239] confirms that the topic of exercise is not discussed in more than half of cancer treatment consultations. In the UK despite a very favourable attitude towards offering exercise rehabilitation within National Health Service hospitals, [69] provision of patient exercise rehabilitation services is rare. The lack of resources, expertise and awareness of the benefits of exercise for cancer patients as confirmed by a recent survey of health professionals in 2005 [69] would suggest that the opportunity for appropriate advice is not reaching those cancer patients in need of exercise information and support, thereby highlighting health professionals training needs.

Work by Emslie and colleagues (2007) [230] concurs with information found in this study, that women who did initiate attempts at exercise post-treatment had experienced a difficult return to exercise, or as Emslie describes "feelings of demoralisation". The expectation of personal health benefit is one of the key incentives to exercise in women with breast cancer.[221,235] Previous research reveals the top four anticipated benefits of exercise in breast cancer patients during treatment to be physically related benefits; improving heart and lungs, improving health/reducing disease risk, increasing muscle strength and losing weight.[220] The same research demonstrates that the benefits considered most important and therefore most desirable, included improving state of mind, reducing tiredness, avoiding injury and improving self-esteem. The authors conclude that anticipated psychological benefits were judged to be more important than the physical

ones. Recent evidence reports that rhythmic exercise such as brisk walking, jogging and cycling and resistance exercise are effective in reducing mental health illness (for example depression and stress disorders) and is effective in promoting positive mental health, such as feeling happier and more satisfied with life.[65]

In a previous trial that randomised breast cancer patients to a 15 week cycling intervention, [170] it was reported that 90.4% of patients thought it extremely or quite likely that exercise would improve well-being and make them feel fitter and 98% expected the exercise would be beneficial, furthermore 80% anticipated that exercise would be enjoyable. Similar expectations of physical benefit were voiced in the current study, but participants did not think that exercise would necessarily be an enjoyable experience.

8.5.2 ACCEPTABILITY

The exercise sessions proved to be tolerable, manageable and enjoyed by participants. There was universal approval for exercise rehabilitation post treatment. Two UK based exercise studies with breast cancer patients [230] and mixed cancer patients [222] have reported that participants were similarly appreciative of having a variety of exercise and equipment and valued the specialist exercise instruction on offer, as was the case in this study. Participants were appreciative of the opportunity to make choices as to which piece of equipment they would use and liked the fact that they had some control of determining their exercise progression. These feelings of self-determination or feelings of being in control, are considered an important construct in the development of intrinsic motivation, [240] which may be an important tool in enabling participants to sustain their exercise participation in the future. Therefore promoting feelings of competence and control should be part of a client-centred approach. The quality of the delivery of an exercise intervention and instructors sensitivity to patients needs has been highlighted as crucial to an interventions success.[188] The instructor's ability to pitch the exercise at the

right level and for participants to be able to exercise safely and without pain contributed toward enjoyment and intervention adherence. Participants reflected that lack of time and travelling to the exercise venue were the only situational barriers to participants participation, similar barriers have been noted in other studies with cancer patients.[221,235]

8.5.3 PERCEIVED PHYSICAL BENEFITS

This exploratory research demonstrated it was possible for participants to perceive physical benefits associated with exercise participation. Improvement of physical function through increased fitness, increased mobility, generally feeling more confident in their ability to exercise and having more energy to engage in everyday activities were the primary perceived physical benefits in this study. These benefits are likely to have contributed toward the improvement of functional well being and the development of physical self–worth which would be assumed to be important elements in optimising QoL. Interview [222] and focus group [230] data from other exercise interventions in the UK have reported equivalent benefits of reduced fatigue and better physical well-being and research from overseas also consistently demonstrates these health gains.[102,104,109]

8.5.4 PSYCHOSOCIAL BENEFITS

The effectiveness of exercise in accelerating the promotion of psychological well-being in participants was highlighted in this study. This process was facilitated by having a more positive outlook, enhanced mood and spending less time dwelling on the negative associations of having had a cancer diagnosis. The routine of regular outings combined with increases in exercise competence and the realisation that participants could improve their functional capacity translated into a sense of retuning to normality and an overall sense of enhanced well-being. Indeed the participants reported improvement in their ability to perform everyday activities which is likely to have fostered a sense of independence which might have resulted in an enhanced perception of their quality of life.

In this qualitative study exercise resulted in increased feelings of confidence and empowerment to take on new challenges. Previous studies have also interpreted the value of exercise as a vehicle for promoting recovery [230] and it has been characterised as an opportunity for "moving forward".[231] Furthermore, survey data of breast cancer patients who participated in a 15 week cycle intervention reported that their exercise experience had helped them maintain a normal lifestyle, beyond that which was anticipated at the outset of the programme.[170] Additionally, there were increases in attitude toward exercise from pre-randomisation to post intervention. The findings from this study endorse this view, as evidenced by participants having a "different mindset" post-exercise intervention. Similar positive psychosocial benefits of exercise rehabilitation have been observed in other populations with specific conditions or needs, such as, coronary heart disease, smoking cessation.[65]

The psychosocial benefits of other studies that have adopted a group approach to exercise elicited meaningful benefits such as comradeship [233] and shared support.[222,232] This type of benefit was not seen or expected in this study due to the one-to-one format of the exercise intervention. However, when designing exercise rehabilitation programmes practitioners may want to consider the value that a group approach might offer.

8.5.6 CLINICAL IMPLICATIONS

Findings from this research have demonstrated that patient's wishes and expectations of feeling better/fitter can be met though a structured, supervised exercise therapy intervention. Moreover, exercise would seem to provide an ideal medium to promote and facilitate the psycho-social benefits that are needed by this population of women. These findings are particularly encouraging given patients descriptions of their reduced motivational readiness for exercise after their cancer treatment. Women were

receptive to the concept of exercise rehabilitation, yet they needed a "kick start" or "helping hand" to becoming regularly physically active.

On the basis of the participants perspectives in this qualitative study, future exercise programmes may want to actively promote and emphasise the desirable breast cancer related psychological benefits of exercise participation, as well as the more established general physical benefits of exercise. Additionally, it would be prudent to offer reassurance to breast cancer patients that exercise is safe, tolerable and manageable. Exercise programmes that focus upon building confidence slowly, have appropriately skilled empathetic instructors, offer a varied and interesting exercise content, and help patients to find solutions to situational barriers, might stand a good chance of achieving optimal adherence rates. Similar attention also needs to be paid to the issue of sustaining exercise behaviour over the longer term. The key reasons for maintaining exercise participation were noted as the desire to maintain the physical and psychosocial benefits that had been accrued over the course of the study and the utility of exercise in helping with weight management. It would be useful for future research to explore how women who have initiated an exercise programme can be helped to maintain their exercise behaviour. Indeed mention was made of the time commitment of taking part in the study and the difficulty that was sometimes encountered travelling to the exercise facility. These types of concerns need to be addressed by both participants and providers of exercise programmes to effectively provided solutions.

Future research may wish to address the question of what is the optimal length of an exercise programme in order to elicit similar magnitude of effects as seen in this study. If similar effects can be obtained in half the sessions then this has favourable implications for both practitioners, by reducing resource allocation; and for participants by reducing the burden on attendance.

8.5.7 STRENGTHS AND WEAKNESSES

The main strength of this research is that it elicited information from participants that was grounded in their original accounts of taking part in the exercise interventions. This study adds value and a personal dimension to our understanding of the exercise experiences of this population. Qualitative investigation usually relies upon much smaller samples than those found in quantitative research designs. This may cast doubt over the external validity of the inferences drawn from the research. The goal of qualitative research however is not to achieve complete generalisability but rather to find similarities and patterns in the data that can be observed in other settings, the transferability of findings is a more important construct.[241]

The internal validity of the study may have been compromised by the interviewer being the same therapist and researcher that had conducted the exercise interventions with the participants. The possibility that participants may have wanted to express favourable views cannot be disregarded. However, this assumption may be challenged by virtue of the fact that participants did feel able to report the negative aspects (barriers) of the study experience. The validity of the analysis of data was enhanced by two other researchers (in addition to the key researcher) in scrutinising the data and confirming the emergent themes, ensuring interpretation of the data was not biased. Adopting a framework approach to data analysis further enabled a rigorous examination of the data, particularly with respect to making constant comparisons within and across the data set.

8.5.8 CONCLUSIONS

The exercise experiences of women treated for breast cancer, who had taken part in an eight-week exercise intervention were explored in this study. Participants revealed how exercise had contributed to accelerating their perceived physical and psychological recovery. Factors that positively mediated programme adherence and enjoyment included; offering an opportunity for "a kick start", integrating personal choice into the exercise programme, exercising without pain, flexible appointment times, and "pitching the exercise at the right level".

CHAPTER 9. OVERALL CONCLUSIONS

Patients who have received a breast cancer diagnosis and subsequent treatment can experience considerable losses in physiological function and deterioration in psychological well-being. Such effects may have implications for emotional and functional well-being thereby compromising patient's quality of life (QoL).

The role and value of exercise therapy as an aid to promoting adjustment in breast cancer patients has not yet been fully researched and explored in the United Kingdom (UK). The primary aim of this study was to investigate the impact of exercise therapy upon quality of life (QoL) in women who were in the recovery phase of the cancer experience, following the completion of breast cancer treatment. It is hoped that this body of work will be a valuable addition to the limited existing evidence-base with respect to the value of exercise rehabilitation post-breast cancer treatment. Worthwhile findings arising from the main study regarding trial recruitment and intervention adherence emerged. A valuable opportunity stemming from the trial arose, to investigate participants' personal reflections upon taking part in novel therapeutic exercise interventions. The key findings of the project are summarised below followed by thoughts regarding future topics for research in this field.

9.1 EFFECTS OF EXERCISE

A supervised aerobic exercise therapy-based intervention, lasting eight weeks provided participants with QoL benefits that were of clinical benefit (chapter 4). Measures of depression, perceptions of physical self-worth and physical conditioning, aerobic fitness and intention toward sustaining exercise behaviour were also favourably influenced by taking part in moderate intensity exercise therapy. A low intensity exercise-placebo intervention that focussed upon flexibility and light toning exercises also demonstrated modest potential to positively influence some components of psychological well-being.

It was encouraging to find that an exercise therapy intervention of even short duration was able to promote positive adjustment to the cancer experience. In particular this study highlighted the unique potential of exercise to address both functional limitations and to attenuate symptoms of psychological distress, such as depression and low physical self-worth that are often concomitant with breast cancer treatment. Equally encouraging was the finding that fatigue was not exacerbated by taking part in exercise. In light of these findings the maxim "rest is best" may be put to bed. Collectively the evidence from this study lends support to the recommendations that patients should aim to resume or initiate exercise participation post breast cancer treatment to optimise their recovery and subsequent QoL.

9.2 FEASIBILITY OF EXERCISE

Participants recruitment into the trial (see chapter 6) represented an on-going challenge, which potentially could be a similar concern in future randomised controlled trials involving clinical populations. Despite dedicated support from treating oncologists inviting screened women to take part in the study, it was necessary to draw upon the considerable reach and immediacy of community recruitment strategies such as local press and television to access potential participants. On the basis of clinician invitation it does seem that affluent women treated for breast cancer are more likely to respond than their less affluent counterparts. Demographic, socio-economic characteristics, lifestyle and cancer treatment related variables were not however, related to route of recruitment into the study. These findings highlight the need to actively target as many patients as possible through a diverse range of promotional strategies. For future studies, utilising the support of local external agencies to access patients from within the cancer/health care system and outside of this context might prove advantageous.

Exercise session adherence (chapter 7) to both interventions was excellent and they proved to be tolerable and acceptable to women treated for breast cancer. The findings also indicate that participants had the physical capacity to exercise at a moderate intensity. Nonetheless, findings demonstrate that exercise adherence is susceptible to fluctuations in attendance thereby reflecting the busy lifestyles of many women treated for breast cancer who are integrating their recovery with everyday responsibilities and activities. As this was an efficacy study the structured, supervised exercise sessions at a facility not local to the participants may have created it's own situational barriers toward exercise participation. Indeed mention was made of the time commitment of taking part i the study and the difficulty sometimes encountered travelling to the exercise facility. Further research is needed to identify all the potential determinants of exercise adherence in this population. Designing interventions to enhance regular and sustained exercise remains a challenging proposition.

9.3 EXPERIENCES OF EXERCISE

The qualitative investigation (see chapter 8) revealed that participants in both the exercise interventions were apprehensive about their physical capacity to undertake exercise training. Further, they did not want to exacerbate any existing breast cancer related lymphoedema which combined with deterioration in their physical condition and feelings of low mood meant they often found it difficult to find the motivation to initiate exercise on their own. Lack of professional exercise advice from within the health care setting exacerbated this feeling. Participants were therefore appreciative of the opportunity of a helping hand to initiate an exercise routine. Participants revealed how taking part in exercise had contributed to accelerating their perceived physical and psychological recovery breaking a cycle of low self-esteem and feelings of low confidence. The patient-centred approach undertaken within this study was valued and fostered enjoyment and

compliance to the interventions. This type of evidence grounded in the participants' experiences provided useful information from which practitioners can tailor promotional messages regarding the efficacy of exercise rehabilitation and the optimal design of interventions to meet participants' preferences.

9.4 RECOMMENDATIONS FOR FUTURE RESEARCH

As a result of undertaking this study some areas for future research have emerged. QoL benefits are central to facilitating recovery in breast cancer patients. Future work that can determine the optimal timing of an exercise rehabilitation intervention for breast cancer patients would be an important contribution to help establish the efficacy of exercise in promoting positive adjustment. It could be that a critical period for exercise rehabilitation exists within a certain number of months post-treatment. It is unknown whether the efficacy of exercise in maintaining QoL remains for a period of years after breast cancer treatment.

Recruitment in to the study was slower than had been anticipated and therefore more information is needed to understand the determinants of breast cancer patient's decisions to engage or not in exercise, whether it be in the context of a trial or via self-initiated participation. Identifying factors that influence exercise motivation and the barriers to exercise participation is certainly an under-researched topic in cancer populations in the UK.

Maintenance of health benefits gained through exercise requires sustained exercise behaviour. Defining trials and exercise interventions that can support longer lasting improvements in QoL will be one of the key issues for future research to address. Investigating a more pragmatic approach to programme delivery, such as home-based interventions or integrating the concept of new technology (such as internet and multi-media resources) to facilitate exercise behaviour change may be an important advance.

Consideration must also be given to determining the cost-effectiveness of various types of exercise interventions. Equally important will be testing the feasibility of integrating exercise provision into mainstream cancer care.

To date most exercise intervention studies have been focussed upon breast cancer patients. There is a need to focus future attention upon other cancer populations. The relative merits of exercise rehabilitation for breast cancer patients might not be transferable to patients with other cancer types such as colo-rectal, prostate and lung. It could be that exercise modalities and exercise prescriptions need to be tailored not only to individuals but also to cancer type and treatment regimes. Further work that aims to discover the mechanisms underpinning cancer related fatigue and can characterise its nature from the patient perspective, across various time points in the recovery process, may offer a better chance of delivering effective exercise solutions that may combat fatigue.

CHAPTER 10. IMPLICATIONS FOR PRACTICE

Due to the sparsity of exercise intervention studies in the UK with breast cancer patients, there is a lack of practical advice for researchers and health professionals to refer to for guidance. The following observations have been drawn from the experience of conducting this trial and could be of benefit to those individuals who are planning to implement exercise rehabilitation for post treatment breast cancer patients.

10.1 LEVEL OF INTERVENTION SUPPORT

The exercise interventions within this study were run on a one-to one basis with a qualified exercise instructor. This intensive approach has merit in that a great deal of of attention can be paid to the individual, this is advantageous in the early stages of exercise adoption when novice exercisers require a concentrated period of support to learn the basics of exercise technique; this period may however, need only be brief if exercises and types of equipment are kept to a minimum. Exercise programmes that incorporate more diverse exercise modalities and include exercise progressions will require a greater level of ongoing tutorial support. It is also useful to have exclusive time with an individual to conduct some aspects of exercise counselling. Conducting an exercise trial or offering exercise sessions on a one-to-one basis is likely to be beyond the remit of most clinical and health service resources, as it is very time-consuming (the current study involved over 2000 hours of one-to-one contact time with patients) and as such will have implications for the cost-effectiveness of any intervention offered. Recent UK-based studies have found that exercise carried out in a group setting created a sense of shared purposefulness and furthermore participants considered the group cohesion to be a valuable asset of the exercise programme.[222,230] From a practical perspective it would make sense to offer any future exercise intervention on a group basis. However, it should be noted that if

psychological well-being outcomes are to be assessed in relation to exercise participation it may be necessary to control for group dynamics and interaction.

10.2 EXERCISE PROGRAMMING CONSIDERATIONS

Practitioners should be aware that it is imperative to closely monitor the intensity at which participants are exercising, this is particularly important when a defined exercise prescription or intensity level has been set (i.e. moderate intensity). Some participants may be over enthusiastic and inadvertently exercise beyond the prescribed exercise dose or conversely, others may not be reaching a minimum requirement. These type of tendencies have been observed in multiple sclerosis patients.[242] Considerable attention should be paid to educating participants how to monitor exercise intensity for example, via Rating of Perceived Exertion (RPE) and how to safely perform exercises with correct technique and to understand the principles of exercise progression.

Practitioners should aim to adopt not only a breast cancer specific approach to exercise prescription taking into account the severity of breast cancer related symptoms and limitations, but also consider a holistic approach that takes into consideration existing co-morbid conditions (i.e. hypertension, osteoporosis, diabetes, arthritis).[243] It is important for practitioners to consider any contra-indicated exercises, with particular reference to breast cancer related lymphoedema. Asking participants for feedback in response to their exercise prescription and continual monitoring of signs and symptoms is vital when working with participants who may be at risk of metastatic disease and for those patients who are post-surgical treatment and may be at risk of oedema. This type of approach calls for practitioners who have both an exercise background and a specific understanding of the type of cancer, treatment modalities, treatment toxicities and complications and subsequent implications for exercise.[244]

10.3 PROMOTING EXERCISE ADHERENCE

The current study achieved very good adherence rates for both exercise therapy and exercise-placebo interventions. This was partly due to exercise sessions being offered on a very flexible basis, in response to patient requests. It might be possible to offer convenient exercise schedules, incorporating morning, evening and weekend sessions on a more formalised basis. Practitioners should be aware that after treatment breast cancer patients are likely to be either in employment or have child care/family responsibilities.

Offering participants choice and involvement in their exercise programming, alongside the promotion of feelings of competence and control are likely to foster better compliance towards an exercise intervention or recommendations. It is also worth practitioners taking time to become aware of and explore participant's perceived "roadblocks" toward exercise. These may stem from existing attitudes, apprehensions and concerns about physical capacity to exercise. Participant's appraisal of exercise attitudes and priorities might be facilitated by exercise counselling sessions. Adopting an exercise counselling approach that takes into account the cognitive and behavioural aspects of becoming more active and sustaining that behaviour has been shown to have considerable value and success.[245,246] However, it is worth noting that not all participants will be receptive toward sitting down and thinking through their exercise participation. Participant preferences for exercise counselling vary. Furthermore it is necessary to work at the participants pace and re-visit counselling topics, as and when it is appropriate for the individual, so some degree of flexibility is needed within the exercise counselling framework. Practitioners will find benefit in adopting an empathetic style and utilising reflective listening skills to aid their communication with participants.

10.4 NEW DIRECTIONS FOR PRACTICE

Advising breast cancer patients to become more active upon completion of their treatment would be a departure from current practice of no advice or advice based upon the principle of "rest is best". Current provision of exercise rehabilitation services within the continuum of cancer care in the U.K. is rare. Implementing exercise recommendations and policy will require a change in clinical practice, which will demand appropriately qualified and trained personnel.

The benefits of exercise are typically framed in physical terms, for example, helping to lose weight and feeling fitter-which are salient and relevant benefits to breast cancer patients. It may also be worthwhile to promote the psycho-social benefits of aerobic exercise to this population, such as improvements in physical self-worth, feelings of improved confidence, and feelings of "getting back to normal". These may be lesser anticipated, yet very appealing benefits to breast cancer patients. Similarly offering reassurance that exercise participation can be safe, tolerable and effective would be a useful initial promotional strategy.

10.5 PRACTITIONER IMPLICATIONS

For professionals working with vulnerable populations such as cancer patients it is important to consider the potential for emotional burden to inadvertently fall upon practitioners.[247,248] Cancer diagnosis and treatment can be a traumatic and emotional experience. Participants might wish to "tell their story"; this can present itself in the context of the exercise counselling sessions, or may be referred to in response to the assessment of outcomes such as depression and QoL, or could simply be reflected upon in conversation. Indeed researchers directly ask participants to recall their experiences to answer a variety of questions. Whilst many of these experiences are positive, sometimes participant's reflections are accompanied by emotional distress. Handling this type of

distress and offering the appropriate level of support requires a degree of expertise. Thus it would be prudent to set in place mechanisms for practitioner training and support. It is also possible that practitioners might need to refer participants to specialist professionals such as psychiatrists, dieticians and physiotherapists. The tools that help to identify participants who are in need of further specialist assistance need to be in place and referral mechanisms to members of a multi-disciplinary teams should be set up.

There exists a valuable opportunity for health professionals to provide lifestyle education/health promotion to breast cancer patients after their cancer treatment. Timely and relevant intervention could help women to manage their rehabilitation from breast cancer treatment and hasten their recovery.

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APPENDICES

Appendix 1

Trial Outline

the Centre for sport and exercise science

Sheffield Hallam University

Sheffield Women's Exercise and Health Project

What is the project about?

Recovering from breast cancer can be a difficult experience both physically and emotionally. This project aims to consider whether exercise can help to improve the general health and well-being of women who have had breast cancer. Women who have completed some form of cancer treatment (a minimum of one year and a maximum of three years) prior to starting the project are invited to participate.

What is involved?

Participants are allocated to one of three groups outlined below. It is important to understand that participants are allocated to one of the three groups by random.

Group 1: Participants are asked to follow an individualised and progressive exercise programme, with one-to-one supervision from an exercise specialist, three times per week for eight weeks. Participants are offered a range of activities and asked to exercise at moderate intensity. Strategies that help participants to maintain their exercise in the long-term will also be explored during the exercise sessions.

Group 2: Participants in this group are offered body conditioning exercises; these will include stretching, body control, toning and strengthening exercises. Participants are required to attend the Centre for three exercise sessions per week, for eight weeks. Each session will be on a one-to-one basis with an exercise specialist

Group 3: Participants in this group do not participate in any exercise sessions at the Centre, but simply continue their lives as normal. At the end of the project, participants in this group will be offered an exercise consultation and personalised exercise plan.

Throughout the course of the project participants will be asked to complete a series of questionnaires about their general health and well-being. Fitness (walking), muscle strength, height and weight are also measured.

Where does the project take place?

At the Centre for Sport and Exercise Science, Sheffield Hallam University, Ecclesall Road. This project is generously supported by Cancer Research UK.

Participants will receive £2.50 per visit towards travel expenses to the Centre. All participants will receive a £20 sports shop voucher at the end of their involvement in the project.

For further information contact Helen Crank on 0114 225 5572 Email H.Crank@shu.ac.uk

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Appendix 2

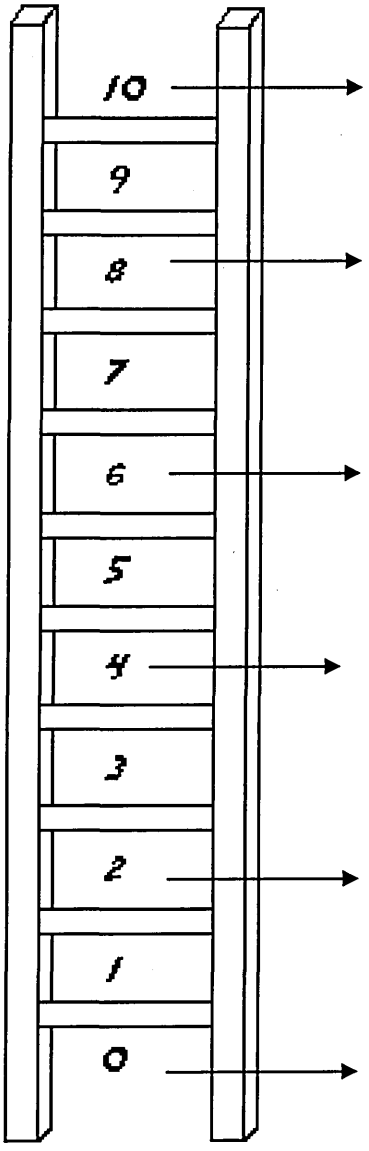
Stage of Change for Exercise

Physical Activity and You.

We would just like to find out how physically active you are at the moment.

1. Please circle the **number on the ladder** that best describes your levels of activity. Please answer this question as honestly as you can.

*Regular exercise = three or more times per week for 20 minutes or longer of moderate exercise e.g. walking briskly or cycling, swimming.



10 — I exercise regularly* and have done so for longer than 6 months.

8 — I exercise regularly* but have done so for less than 6 months.

6 — I currently exercise some, but not regularly*

4 — I have exercised in the past 6 months but have not done so recently

2 — I currently don't exercise but I am thinking about starting in the next 6 months

0 — I currently don't exercise and I do not intend to start in the next 6 months

2. How **often** have you participated in physical activities for 20 to 30 minutes per session during your free time in the last three months? Please tick one box.

never ☐

about once per month ☐

about 2 or 3 times per month ☐

about 4 times or more per week ☐

about once per week ☐

about 2 times per week ☐

about 3 times per week ☐

Appendix 3

Patient Information Sheet

Exercise therapy in women who have been treated for breast cancer

Information Sheet

Version 3: 18th August 2003

You are being invited to take part in a research project. But before you decide whether you would like to take part it is important for you to understand why the research is being conducted and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish.

Ask us if there is anything that is not clear or if you would like more information. Please take your time to decide whether or not you wish to take part.

Consumers for Ethics in Research (CERES) publish a leaflet entitled "Medical Research and You". This leaflet gives more information about medical research and considers some of the questions you may want to ask. A copy can be obtained from CERES, PO Box 1365, London, N16 0BW.

In order to make sure that you have some general information about this study we have compiled a list of questions and answers. We hope that this will allow you to make an informed decision as to whether you would like to become involved in this project.

Q: What is the purpose of this study?

A:. Recovering from breast cancer can be a difficult experience both physically and psychologically for many women. This research project will consider whether exercise can help to improve the general health and well-being of women who have had breast cancer. We hope that this study will provide health professionals with information regarding the usefulness of exercise in women who have been treated for breast cancer. Your involvement in the study will last 8 months.

Q: Why have I been chosen?

A: In order to take part in this study you must have completed some form of breast cancer treatment within 12 months and no longer undergoing active treatment. Women who live in Sheffield and who fulfil this criteria are being invited to participate in this project.

Q: Do I have to take part?

A: It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This will not affect the standard of care you receive from the Weston Park or Royal Hallamshire Hospitals or any other health professional.

Q: What will be involved if I agree to take part in the study?

A. Once the consent form has been signed you will be asked to participate in one of 3 groups. The requirements of each of these groups are outlined below. It is important to understand that you will be allocated to one of the 3 groups in a random order. We have to do this in order to make sure the results are scientific.

Over the course of the study we would like you (irrespective of which group you are in) to complete a series of questionnaires that will ask you to indicate your feelings about your general health and well-being. We will also assess you fitness (walking), muscle strength and body fat. You may be asked to participate in a short interview asking you about your feelings regarding your exercise participation in the study. This interview would be video and audio taped. All responses will be anonymised.

Group 1: Exercise therapy

The exercise sessions will take place within the Centre for Sport and Exercise Science at Sheffield Hallam University. If you are randomly allocated to this group, you will be offered a range of exercise types and asked to exercise at moderate intensity for 30 minutes 3 times per week for 8 weeks. All exercise sessions will be on a 'one-to-one' basis with an exercise specialist/researcher. An important feature of each exercise session will be exercise counselling where the exercise specialist will encourage you to discuss your thoughts and feelings about exercise and other aspects of your lifestyle. These sessions will last for 50 minutes. If for any reason you feel that you are not able to exercise you should inform the exercise specialist.

Group 2: Body conditioning classes

Similar to the exercise therapy, the conditioning sessions will occur 3 times per week for 8 weeks and last for 50 minutes. The conditioning sessions will focus upon flexibility, body control, and range of motion, stretching and posture through the use of a mini-circuit of exercises. If you are assigned to this group, you will be asked to continue your exercise participation as normal.

Group 3: Comparison Group

If you are allocated to this group, you will not take part in exercise therapy or body conditioning but will be asked to visit the Centre at various times throughout the duration of the study to complete a series of questionnaires and a walking test. We will also assess your muscle strength and body fat. Three months after the completion of your involvement in the study, you will be asked to visit the Centre for a final assessment (questionnaires, walking test etc). Throughout the course of the study you should continue to live your life as normal.

Q: What are the side effects?

A: Sometimes when people have not exercised for a long time they can experience shortness of breath during exercise and muscle soreness after exercise. If you suffer from epilepsy, asthma or diabetes you should inform the exercise researcher before taking part in the study.

Q: What are the possible benefits of taking part?

A: If you are assigned to the exercise therapy group, you will be able to take part in supervised exercise 3 times per week for 8 weeks and you will be given additional help and guidance regarding you health and lifestyle. If you are assigned to the body conditioning

group, you will be given advice about posture, flexibility and range of motion in your joints. If you are assigned to the control group, we will give you advice about exercise at the end of your involvement in the project, if you wish.

Q: Can I withdraw from the study at any time?

A: Yes you can. You are free to refuse to join the study and may withdraw at any time or choose not to answer certain questions. You will receive the same quality of care from the hospital whether you join the project or not. If you think you might be pregnant you should inform the exercise researcher.

Q: When and where will the project take place?

A: The exercise therapy and body conditioning sessions will be based at the Centre for Sport and Exercise Science at Sheffield Hallam University. Your travel expenses will be reimbursed (£2.50 per visit).

Q: What other information will be collected in the study?

A: With your agreement, we may wish to obtain additional information about the type of treatment you received at the Weston Park or Royal Hallamshire Hospitals, and your hospital admissions from your medical records. This would be done via the Cancer Research Centre at Weston Park Hospital.

Q: Will there be any effects on my follow-up screening?

A: No, your participation in the study is not connected to your follow-ups.

Q: What happens when the research stops?

A: Once you have completed the first 8-weeks of the study you will be given advice about how to exercise safely on your own. You may choose to join your local gym or exercise club. The exercise specialist will give you help regarding this issue nearer the time.

Q: Will the information obtained in the study be confidential?

A: Anything you say will be treated in confidence. Your name will not be mentioned in any reports of the study and care will be taken so that you cannot be identified from details in reports.

Q: Will anyone else be told about my participation in the project?

A: With your agreement, we will inform your family doctor that you are helping with this study.

Q: What will happen to the results of the research project?

A: We hope to publish the findings from this project in appropriate health science research journals. The data may also be presented at conferences. Only individuals who are directly related to this project will have access to the research data. All data will be kept in a locked cupboard.

Q: Who is organising and funding the research?

A: The study is been conducted by the Centre for Sport and Exercise Science at Sheffield Hallam University, in conjunction with the Cancer Research Centre, Weston Park Hospital. Cancer Research UK has provided the funding for this project.

Q: Who has reviewed the study?

A: The South Sheffield Research Ethics Committee has approved this study.

Q: What if I wish to complain about the way in which this study has been conducted

If you have any cause to complain about any aspect of the way in which you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you and are not compromised in any way because you have taken part in a research study.

If you have any complaints or concerns please contact either the project co-ordinator:

Name: Dr Amanda Daley..... Tel: 0114 225 4426.....EITHER

Otherwise you can use the normal hospital complaints procedure and contact the following person:

Name: Chris Welch..... . Tel: 0114 271 2178.....

OR

Otherwise you can use the normal University complaints procedure and contact the following person:

Name: Office of the Registrar .. Tel: 0114 225 5555.

Sheffield Hallam University has the following policies in place for the legal liability of the University; (a) Professional indemnity (£10 million); and (b) Public liability (£20 million).

Thank you for taking the time to consider your participation in this study. Dr. Amanda Daley (Project Co-ordinator)

CANCER RESEARCH UK

CONSENT FORM

Title of Project: The effects of exercise therapy upon quality of life in women who have been treated for breast cancer

Name of Researcher: Dr. Amanda Daley / Helen Crank

Please Initial box

1. I confirm that I have read and understood the information sheet dated ..... for the above project and I have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical or legal rights being affected. ☐

3. I understand that sections of medical notes may be looked at by responsible individuals where it is relevant to my involvement in this project. ☐

4. I understand that the information will remain confidential. ☐

5. I agree to take part in the above project.

Name of Participant	Date	Signature
Name of Person taking consent (if different from researcher)	Date	Signature
Researcher	Date	Signature

Appendix 5

Physical Activity Readiness Questionnaire & Medical Screening

Participant Details and Medical Screening

(including the PAR-Q Questionnaire)

Name:_____

Address:_____

_____

_____

Date of birth_____

Oncologist / Surgeon / Consultant_____

Hospital _____

Your own GP name and address_____

_____

Breast Care Nurse_____

Date of Diagnosis_____

Stage of breast cancer _____

Type of treatment _____

_____

_____

(Surgery - type, radiotherapy, chemotherapy)

Date treatment completed _____

Have you or do you suffer from Lymphoedema?

_____
_____

1.Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?

_____
_____
_____

2.Are you taking any medication for blood pressure or a heart condition?

_____
_____

3.Do you feel pain in your chest when you do physical activity?

_____
_____

4.In the past month, have you had chest pain when you were not doing physical activity?

_____
_____

5.Are you currently taking any other medication?

(name, for)_____
_____

Dosage?_____

Any side-effects? _____

6.Do you experience headaches or migraines? How often?

_____
_____

7.Do you lose your balance due to dizziness or do you ever lose consciousness? (epilepsy, fits)

_____

_____

8.Do you have a bone or joint problem which could be made worse by a change in your physical activity? (including back pain / problems)

_____

_____

_____

9.Have you undergone any surgical operations or experienced any injuries?

(recurrent problems)_____

_____

_____

10.Do you have or have you previously had any of the following medical conditions: please tick the box if you do;

Asthma ☐ Diabetes ☐ Hernia ☐ Heart Murmur ☐

Stroke ☐ Gout ☐ Liver or Kidney problems ☐

High blood Pressure 140/90 ☐ Raised cholesterol ☐

11.Are you pregnant Yes ☐ No ☐

Is it your intention to become pregnant within the next three months?

Yes ☐ No ☐

12.Do you know of any reason why you should not do physical activity?

_____

_____

13.Do you smoke? No ☐ Yes ☐ How many per ____day / ____week?

_____

_____

14. How many units of alcohol do you drink per week?_____

_____

Resting Blood Pressure

_____

_____

Resting Pulse_____

SAFETY AGREEMENT

I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction.

I acknowledge that there are risks and dangers inherent in physical exercise and declare that I know of no reason why I should not take part in moderate exercise.

I understand that any exercise taken is at my own risk and I agree to waive any legal recourse (other than for negligence) for any damages to myself arising from my participation. I also agree to follow any verbal instructions given by the exercise specialist and to observe any written notices regarding safety whilst visiting the facilities at The Centre for Sport and Exercise Science.

Signed by participant:_____ **Date:**_____

Appendix 6

Functional Assessment of Cancer Therapy – General (FACT-G)

YOUR WELL-BEING

Below is a list of statements that other people who have experienced breast cancer have said are important. **By circling one number per line, please indicate how true each statement has been for you during the past 7 days.**

PHYSICAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
I have a lack of energy	0	1	2	3	4
I have nausea	0	1	2	3	4
Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
I have pain	0	1	2	3	4
I am bothered by side effects of treatment	0	1	2	3	4
I feel ill	0	1	2	3	4
I am forced to spend time in bed	0	1	2	3	4

SOCIAL/FAMILY WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
I feel close to my friends	0	1	2	3	4
I get emotional support from my family	0	1	2	3	4
I get support from my friends	0	1	2	3	4
My family has accepted my illness	0	1	2	3	4
I am satisfied with family communication about my illness	0	1	2	3	4
I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please check this box ☐ and go to the next section.					
I am satisfied with my sex life	0	1	2	3	4

By circling one number per line, please indicate how true each statement has been for you during the past 7 days.

EMOTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
I feel sad	0	1	2	3	4
I am satisfied with how I am coping with my illness	0	1	2	3	4
I am losing hope in the fight against my illness	0	1	2	3	4
I feel nervous	0	1	2	3	4
I worry about dying	0	1	2	3	4
I worry that my condition will get worse	0	1	2	3	4

FUNCTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
I am able to work (include work at home)	0	1	2	3	4
My work (include work at home) is fulfilling	0	1	2	3	4
I am able to enjoy life	0	1	2	3	4
I have accepted my illness	0	1	2	3	4
I am sleeping well	0	1	2	3	4
I am enjoying the things I usually do for fun	0	1	2	3	4
I am content with the quality of my life right now	0	1	2	3	4

By circling one (1) number per line, please indicate how true each statement has been for you during the past 7 days.

ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
I have been short of breath	0	1	2	3	4
I am self-conscious about the way I dress	0	1	2	3	4
One or both of my arms are swollen or tender	0	1	2	3	4
I feel sexually attractive	0	1	2	3	4
I am bothered by hair loss	0	1	2	3	4
I worry that other members of my family might someday get the same illness I have	0	1	2	3	4
I worry about the effect of stress on my illness	0	1	2	3	4
I am bothered by a change in weight	0	1	2	3	4
I am able to feel like a woman	0	1	2	3	4
I have certain parts of my body where I experience significant pain	0	1	2	3	4

WHAT AM I LIKE

Here are statements which allow people to describe themselves. There are no right or wrong answers. Please read the entire sentence across. *First* decide which one of the two parts of each statement ***best*** describes you and then go to that side of the statement and tick whether that is just ***sort of true*** or ***really true*** for you. You will tick ONE of the four boxes for each statement.

	Really True for me	Sort of True for me				Really True for me	Sort of True for me
1	☐	☐	Some people feel that they are not very good when it comes to playing sports	**BUT**	Others feel that they are really good at just about every sport	☐	☐
2	☐	☐	Some people are not very confident about their level of physical conditioning and fitness	**BUT**	Others always feel confident that they maintain excellent conditioning and fitness	☐	☐
3	☐	☐	Some people feel that compared to most, they have an attractive body	**BUT**	Others feel that compared to most, their body is not quite so attractive	☐	☐
4	☐	☐	Some people feel that they are physically stronger than most people of their sex	**BUT**	Others feel that they lack physical strength compared to most others of their sex	☐	☐
5	☐	☐	Some people feel extremely proud of who they are and what they can do physically	**BUT**	Others are not some times quite so proud of who they are physically	☐	☐
6	☐	☐	Some feel that they are among the best when it comes to athletic ability	**BUT**	Others feel that they are not among the most able when it comes to athletics	☐	☐
7	☐	☐	Some people make certain they take part in some form of vigorous physical exercise	**BUT**	Others don't often manage to keep up regular vigorous physical exercise	☐	☐
8	☐	☐	Some people feel that they have difficulty maintaining an attractive body	**BUT**	Others feel that they are easily able to keep their bodies looking attractive	☐	☐
9	☐	☐	Some people feel that their muscles are much stronger than most of their sex	**BUT**	Others feel that on the whole their muscles are not quite so strong as most others of their sex	☐	☐
10	☐	☐	Some people are sometimes not so happy with the way they are or what they do physically	**BUT**	Others always feel happy about the kind of person they are physically	☐	☐
11	☐	☐	Some people are not quite so confident when it comes to taking part in sports activities	**BUT**	Others are among the most confident when it comes to taking part in sports activities	☐	☐
12	☐	☐	Some people do not usually have a high level of stamina and fitness	**BUT**	Others always maintain a high level of stamina and fitness	☐	☐
13	☐	☐	Some people feel embarrassed when it comes to wearing few clothes	**BUT**	Others do not fell embarrassed by their bodies when it comes to wearing few clothes	☐	☐
14	☐	☐	When it comes to situations requiring strength some people are one of the first to step forward	**BUT**	When it comes to situations requiring strength some people are one of the last to step forward	☐	☐

	Really True for me	Sort of True for me				Really True for me	Sort of True for me
15	☐	☐	When it comes to the physical side of themselves some people do not feel very confident	**BUT**	Others seem to have a real sense of confidence in the physical side of themselves	☐	☐
16	☐	☐	Some people feel that they are always one of the best when it comes to joining in sports activities	**BUT**	Others feel that they are not one of the best when it comes to joining in activities	☐	☐
17	☐	☐	Some people tend to feel a little uneasy in fitness and exercise settings	**BUT**	Others feel confident and at ease at all times in fitness and exercise settings	☐	☐
18	☐	☐	Some people feel that they are often admired because their physique or figure is considered attractive	**BUT**	Others rarely feel that they receive admiration for the way their body looks	☐	☐
19	☐	☐	Some people tend to lack confidence when it comes to their physical strength	**BUT**	Others are extremely confident when it comes to their physical strength	☐	☐
20	☐	☐	Some people always have a really positive feeling about the physical side of themselves	**BUT**	Others sometimes do not feel positive about the physical side of themselves	☐	☐
21	☐	☐	Some people are sometimes a little slower than most when it comes to learning new skills in a sports situation	**BUT**	Others have always seemed to be among the quickest when it comes to learning new sports skills	☐	☐
22	☐	☐	Some people feel extremely confident about their ability to maintain regular exercise and physical condition	**BUT**	Others don't feel quite so confident about their ability to maintain regular exercise and physical condition	☐	☐
23	☐	☐	Some people feel that compared to most their bodies do not look in the best of shape	**BUT**	Others feel that compared to most their bodies always look in excellent shape	☐	☐
24	☐	☐	Some people fee that they are very strong and have well developed muscles compared to most	**BUT**	Others feel that they are not so strong and their muscles are not very well developed	☐	☐
25	☐	☐	Some people wish they could have more respect for their physical selves	**BUT**	Others always have great respect for their physical selves	☐	☐
26	☐	☐	Given the chance, some people are always one of the first to join in sports activities	**BUT**	Other people sometimes hold back and are not usually among the first to join in sports	☐	☐
27	☐	☐	Some people feel that compared to most they always maintain a high level of physical conditioning	**BUT**	Others feel that compared to most they are not as good at maintaining a high level of physical conditioning	☐	☐
28	☐	☐	Some people are extremely confident about the appearance of their body	**BUT**	Others are a little self-conscious about the appearance of their bodies	☐	☐
29	☐	☐	Some people feel that they are not as good as most at dealing with situations requiring physical strength	**BUT**	Others feel that they are among the best at dealing with situations which require physical strength	☐	☐
30	☐	☐	Some people feel extremely satisfied with the kind of person they are physically	**BUT**	Others sometimes feel a little dissatisfied with their physical selves.	☐	☐

YOUR FEELINGS OF FATIGUE (tiredness, weariness).

For each of the following questions, circle the number that best describes the fatigue you are experiencing <u>now</u>. Please make every effort to answer each question to the best of your ability. Thank you very much.

1. How long have you been feeling fatigued? *(tick one response only)*

   a) Minutes ❑
   b) Hours ❑
   c) Days ❑
   d) Weeks ❑
   e) Months ❑
   f) Other *(please describe)* _____

2. To what degree is the fatigue you are feeling now causing you distress?

No distress										**A great deal of distress**
0	1	2	3	4	5	6	7	8	9	10

3. To what degree is the fatigue you are feeling now interfering with your ability to complete your work or school activities?

None									**A great deal**	
0	1	2	3	4	5	6	7	8	9	10

4. To what degree is the fatigue you are feeling now interfering with your ability to visit or socialise with your friends?

None									**A great deal**	
0	1	2	3	4	5	6	7	8	9	10

5. To what degree is the fatigue you are feeling now interfering with your ability to engage in sexual activity?

None									**A great deal**	
0	1	2	3	4	5	6	7	8	9	10

6. Overall how much is the fatigue, which you are experiencing now, interfering with your ability to engage in the kind of activities you enjoy doing?

None									**A great deal**	
0	1	2	3	4	5	6	7	8	9	10

7. How would you describe the degree of intensity or severity of the fatigue which you are experiencing now?

Mild									**Severe**	
0	1	2	3	4	5	6	7	8	9	10

8. To what degree would you describe the fatigue which you are experiencing now as being...

Pleasant **Unpleasant**

0 1 2 3 4 5 6 7 8 9 10

9. **Agreeable** **Disagreeable**

0 1 2 3 4 5 6 7 8 9 10

10. **Protective** **Destructive**

0 1 2 3 4 5 6 7 8 9 10

11. **Positive** **Negative**

0 1 2 3 4 5 6 7 8 9 10

12. **Normal** **Abnormal**

0 1 2 3 4 5 6 7 8 9 10

13. To what degree are you now feeling...

Strong **Weak**

0 1 2 3 4 5 6 7 8 9 10

14. To what degree are you now feeling...

Awake **Sleepy**

0 1 2 3 4 5 6 7 8 9 10

15. To what degree are you now feeling...

Lively **Listless**

0 1 2 3 4 5 6 7 8 9 10

16. To what degree are you now feeling...

Refreshed **Tired**

0 1 2 3 4 5 6 7 8 9 10

17. To what degree are you now feeling...

Energetic **Unenergetic**

0 1 2 3 4 5 6 7 8 9 10

18. To what degree are you now feeling...

Patient **Impatient**

0 1 2 3 4 5 6 7 8 9 10

19. To what degree are you now feeling...

Relaxed **Tense**

0 1 2 3 4 5 6 7 8 9 10

20. To what degree are you now feeling...

Exhilarated **Depressed**

0 1 2 3 4 5 6 7 8 9 10

21. To what degree are you now feeling...

Able to concentrate **Unable to concentrate**

0 1 2 3 4 5 6 7 8 9 10

22. To what degree are you now feeling...

Able to remember **Unable to remember**

0 1 2 3 4 5 6 7 8 9 10

23. To what degree are you now feeling...

Able to think clearly **Unable to think clearly**

0 1 2 3 4 5 6 7 8 9 10

24. Overall, what do you believe is most directly contributing to or causing your fatigue? _____

_____

25. Overall, the best thing you have found to relieve your fatigue is: _____

_____

26. Is there anything else you would like to add that would describe your fatigue better to us? _____

_____

27. Are you experiencing any other symptoms right now?

No

Yes, please describe _____

_____

@ Your Satisfaction with Life

Please circle one number for each statement below:

	No						Yes
1. In most ways my life is close to my ideal :	1	2	3	4	5	6	7
2. The conditions of my life are excellent:	1	2	3	4	5	6	7
3. I am satisfied with my life:	1	2	3	4	5	6	7
4. So far I have got the important things I want in life:	1	2	3	4	5	6	7
5. If I could live my life over, I would change almost nothing:	1	2	3	4	5	6	7

How have you been feeling in the last two weeks?

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the **past two weeks, including today**. Circle the number beside the statement you have picked. If several statements in the group seen to apply equally well, circle the highest number for that group.

1.			**7.**		
	0	I do not feel sad		0	I don't feel I am being punished
	1	I feel sad much of the time		1	I feel I may be punished
	2	I am sad all the time		2	I expect to be punished
	3	I am so sad or unhappy that I can't stand it		3	I feel I am being punished
2.			**8.**		
	0	I am not discouraged about my future		0	I feel the same about myself as ever
	1	I feel more discouraged about my future than I used to be		1	I have lost confidence in myself
	2	I do not expect things to work out for me		2	I am disappointed in myself
	3	I feel my future is hopeless and will only get worse		3	I dislike myself
3.			**9.**		
	0	I do not feel like a failure		0	I don't criticise or blame myself more than usual
	1	I have failed more than I should have		1	I am more critical of myself than I used to be
	2	As I look back, I see a lot of failures		2	I criticise myself for all of my faults
	3	I feel I am a total failure as a person		3	I blame myself for everything bad that happens
4.			**10.**		
	0	I get as much pleasure as I ever did from the things I enjoy		0	I don't have any thoughts of killing myself
	1	I don't enjoy things as much as I used to		1	I have thoughts of killing myself, but I would not carry them out
	2	I get very little pleasure from the things I used to enjoy		2	I would like to kill myself
	3	I can't get any pleasure from the things I used to enjoy		3	I would kill myself if I have the chance
5.			**11.**		
	0	I don't feel particularly guilty		0	I don't cry anymore than I used to
	1	I feel guilty over many things I have done or should have done		1	I cry more than I used to
	2	I feel quite guilty most of the time		2	I cry over every little thing
	3	I feel guilty all of the time		3	I feel like crying, but I can't
6.			**12.**		
	0	I am no more restless or wound up than usual		0	I am no more irritable than usual
	1	I feel more restless or wound up than usual		1	I am more irritable than usual
	2	I am so restless or agitated that it's hard to stay still		2	I am much more irritable than usual
	3	I am so restless or agitated that I have to keep moving or doing something		3	I am irritable all the time

13.			**18.**		
	0	I have not lost interest in other people or activities		0	I have not experienced any change in my appetite
	1	I am less interested in other people of things than before		1a	My appetite is somewhat less than usual
				1b	My appetite is somewhat greater than usual
	2	I have lost most of my interest in other people or things		2a	My appetite is much less than before
				2b	My appetite is much greater than usual
	3	It's hard to get interested in anything		3a	I have no appetite at all
				3b	I crave food all the time
14.			**19.**		
	0	I make decisions about as well as ever		0	I can concentrate as well as ever
	1	I find it more difficult to make decisions than usual		1	I can't concentrate as well as usual
	2	I have much greater difficulty in making decision than I used to		2	It's hard to keep my mind on anything for very long
	3	I have trouble making any decisions		3	I find I can't concentrate on anything
15.			**20.**		
	0	I do not feel I am worthless		0	I am no more tired or fatigued than usual
	1	I don't consider myself as worthwhile and useful as I used to		1	I get more tired or fatigued more easily than usual
	2	I feel more worthless as compared to other people		2	I am too tired or fatigued to do a lot of the things I used to do
	3	I feel utterly worthless		3	I am too tired or fatigued to do most of the things I used to do
16.			**21.**		
	0	I have as much energy as ever		0	I have not noticed any recent change in my interest in sex
	1	I have less energy than I used to have		1	I am less interested in sex than I used to be
	2	I don't have enough energy to do very much		2	I am much less interest in sex now
	3	I don't have enough energy to do anything		3	I have lost interest in sex completely
17.					
	0	I have not experienced any change in my sleeping pattern			
	1a	I sleep somewhat more than usual			
	1b	I sleep somewhat less than usual			
	2a	I sleep a lot more than usual			
	2b	I sleep a lot less than usual			
	3a	I sleep most of the day			
	3b	I wake up 1-2 hours early and can't get back to sleep			

Appendix 11

Theory of Planned Behaviour - Attitude Scale

Your Feelings about Exercise Participation.

Please consider the statement below, then for each scale, choose one score that best describes your feeling about exercise participation.

Statement: For me to participate in regular physical exercise is:

useless **useful**
-3 -2 -1 0 +1 +2 +3
Write your score here_____

harmful **beneficial**
-3 -2 -1 0 +1 +2 +3
Write your score here_____

foolish wise
-3 -2 -1 0 +1 +2 +3
Write your score here_____

bad **good**
-3 -2 -1 0 +1 +2 +3
Write your score here_____

un-enjoyable **enjoyable**
-3 -2 -1 0 +1 +2 +3
Write your score here_____

unpleasant pleasant
-3 -2 -1 0 +1 +2 +3
Write your score here_____

stressful relaxing
-3 -2 -1 0 +1 +2 +3
Write your score here_____

Appendix 12

Theory of Planned Behaviour - Intention & Subjective Norm

Your thoughts on participating in physical exercise

Please circle a number that best describes your response to the statements below.

- My goal is to participate in physical exercise at least 3 times per week every week

1	2	3	4	5	6	7
Strongly agree		Agree	Neutral		Disagree	Strongly disagree

- I intend to participate in physical exercise as much as I can every week

1	2	3	4	5	6	7
Strongly agree		Agree	Neutral		Disagree	Strongly disagree

- I plan to participate in physical exercise at least _____ times per week

---

Please indicate your agreement / disagreement with the statements listed below by choosing a number as a score.

1	2	3	4	5	6	7
Strongly agree		Agree	Neutral		Disagree	Strongly disagree

- Most people who are important to me think I should participate in regular physical exercise

Score:_____

- Most people who are important to me encourage me to participate in regular physical exercise

Score:_____

- Most people who are important to me support me participating in regular physical exercise

Score:_____

Appendix 13

Perceived Behavioural Control Scale

Again, please circle the number that best indicates your response.

- **How much control do you have over participating in regular physical exercise?**

1	2	3	4	5	6	7
very little control		limited control	neutral	some control		complete control

- **For you to participate in regular physical exercise is**

1	2	3	4	5	6	7
extremely difficult		difficult	neutral	easy		extremely easy

- **If I wanted to I could easily participate in regular physical exercise?**

1	2	3	4	5	6	7
strongly agree		Agree	neutral	disagree		strongly disagree

- **How much I participate in regular physical exercise is completely up to me?**

1	2	3	4	5	6	7
strongly agree		Agree	neutral	disagree		strongly disagree

- **How confident are you that you are capable of participating in regular physical exercise?**

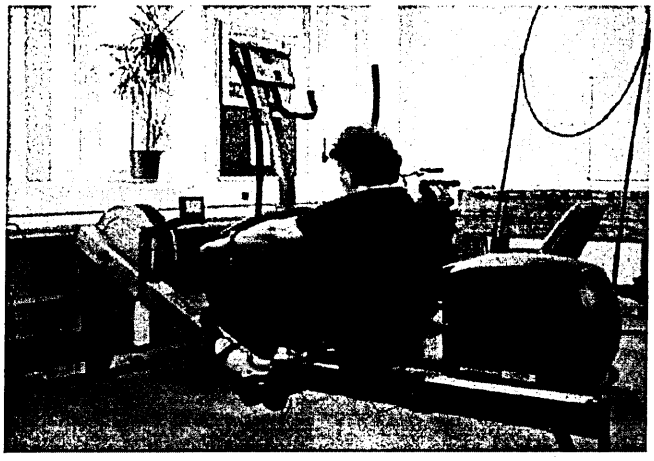
1	2	3	4	5	6	7
not all confident	somewhat confident		neutral	very confident		extremely confident

Appendix 14

Examples of Exercise Therapy Intervention Exercises

Treadmill walking

Elliptical cross-trainer



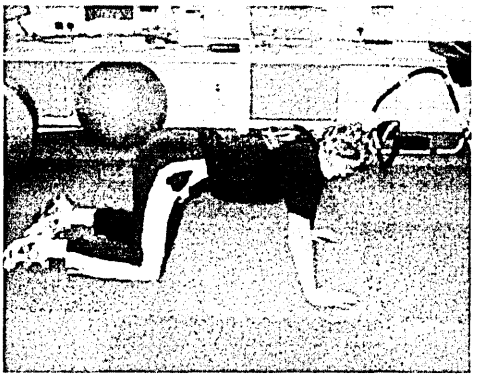
Rower

For further details of the exercise therapy intervention please refer to Chapter 3.

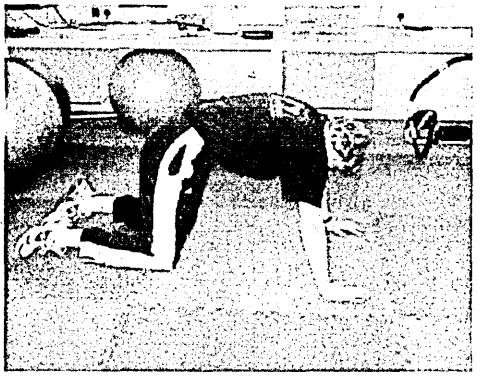
Appendix 15

Examples of Exercise-Placebo Intervention Exercises

Exercise-Placebo Intervention Exercise examples

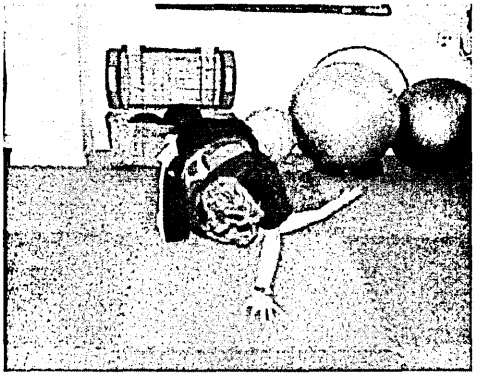


Back flexion

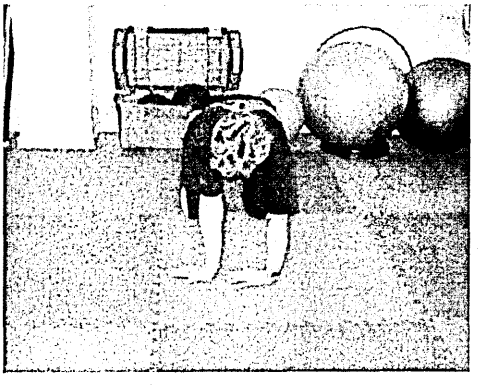


Back extension

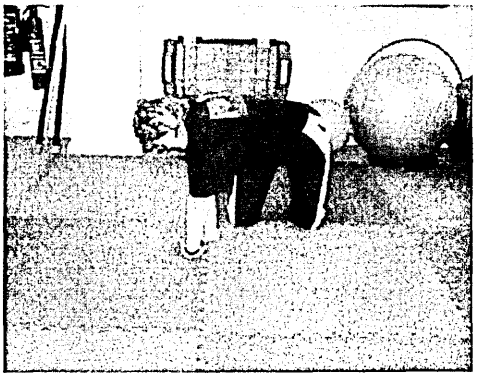
Spinal rotation



Spinal rotation cont.

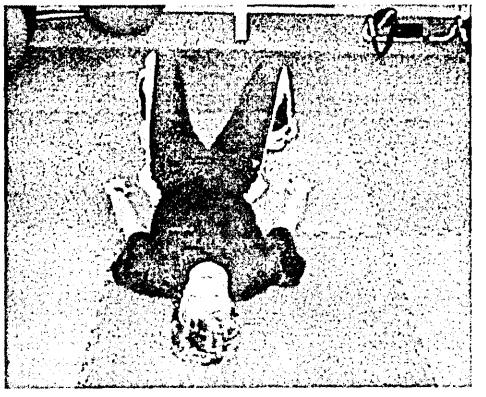


Hand walks (waist stretch)

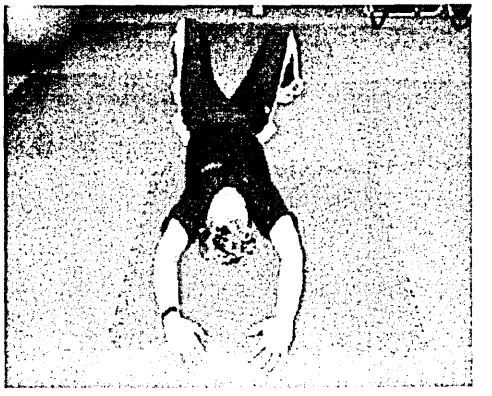


Hand walks cont.

For further details of the exercise-placebo intervention please refer to Chapter 3.

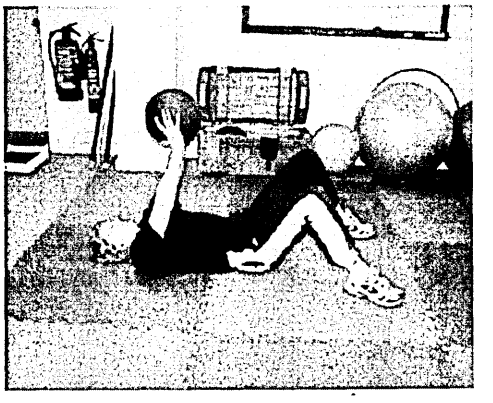


Angel wings (shoulder mobility)

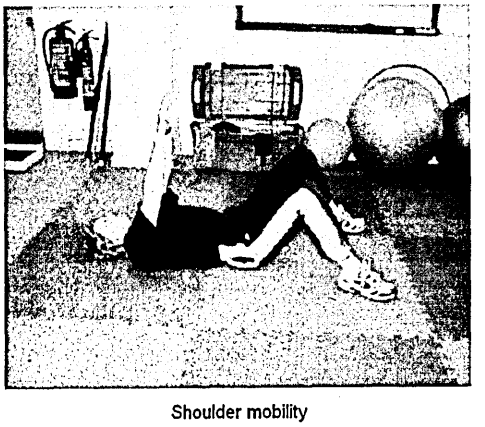


Angel wings cont.

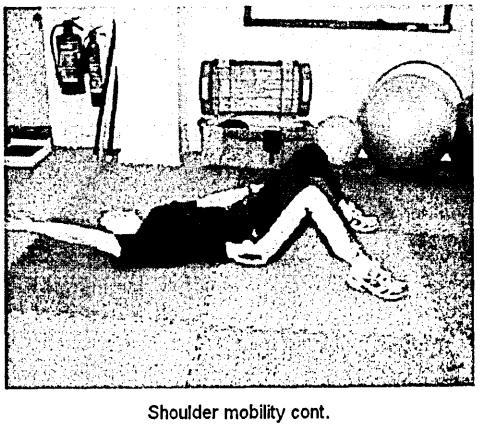
Chest press with ball



Chest press cont.



Shoulder mobility



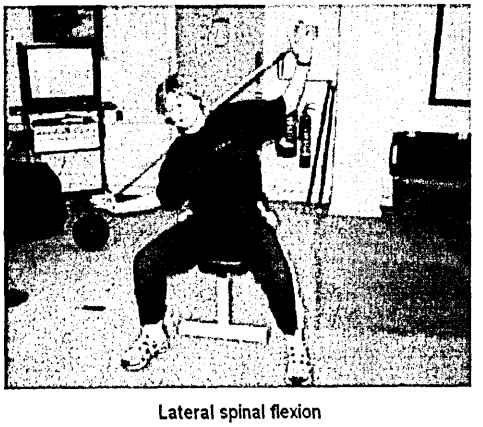
Shoulder mobility cont.

Shoulder press

Shoulder press cont.

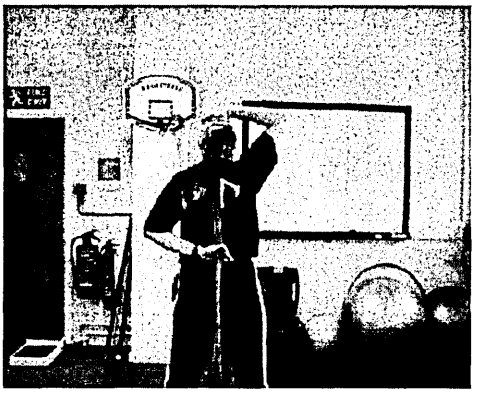
Torso twist standing

Torso twist cont.



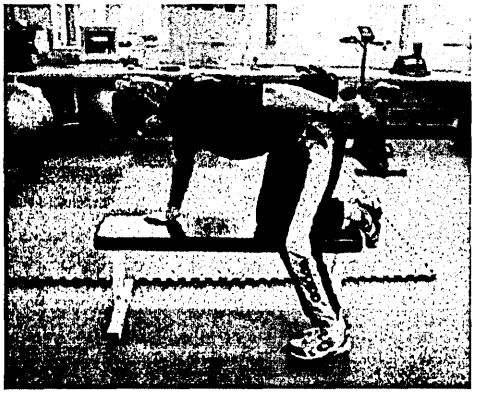
Lateral spinal flexion

Lateral spinal flexion cont.

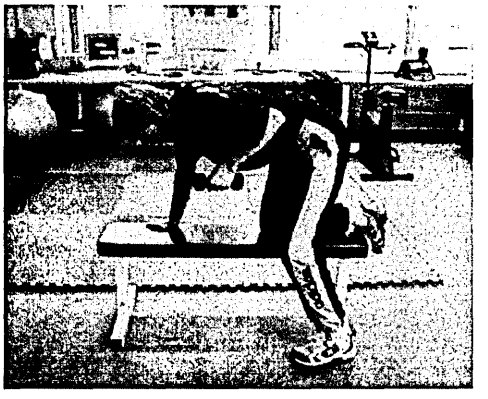


Tricep extension exercise

Tricep extension exercise cont.

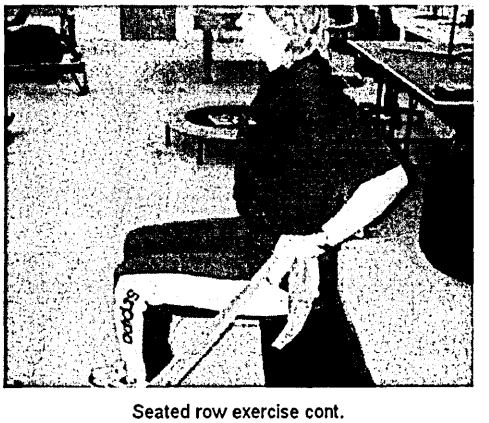


Tricep kickback exercise

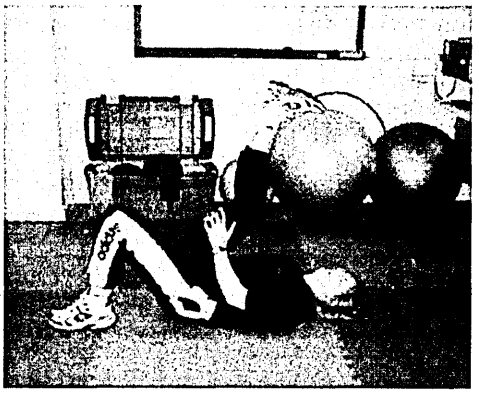


Tricep kickback exercise cont.

Seated row exercise (Mid trapezius)



Seated row exercise cont.



Hamstring stretch (1)

Hamstring stretch (2)

Quadriceps stretch

Hip abductor stretch

Hip abductor & lower back stretch (1)

Hip abductor and lower back stretch (2)

Interview Schedule

Exercise-therapy and exercise-placebo -interview questions after completion of 8 week exercise programme.

Before cancer diagnosis and treatment

Were you regularly physically active prior to your diagnosis and treatment?

Do you remember what your thoughts/perceptions were about exercise?

Once you had finished your treatment

How did you feel after your treatment had finished?

Your health, well-being?

Did you ever think you might like to start exercising?

Yes/No - Why was that?

Did you have any intentions towards exercise?

Did you feel like you were capable / ready to start exercising?

Physical, mental well-being?

What were your thoughts about exercising?

What sort of exercises did you think you might try?

Did you expect exercise to be difficult or easy?

What stopped you from trying exercise?

Physically/mentally/barriers/no exercise knowledge

What motivated you or what you encouraged you to give it a go?

Exercise sessions at the centre

Why did you choose to get involved in the study?

Did you enjoy the sessions? If yes - what did you enjoy/like most?

Was there anything you didn't enjoy about the exercise sessions or coming to the centre? time, effort, motivation, too structured

Were the exercise sessions as you expected? more/ less difficult/ content

Were the exercise sessions something you looked forward to or were they something you felt were an extra burden?

Do you feel confident in your own ability to exercise?

Do you know how hard the exercises should feel in order for it to be doing you some good?

What, if anything have you got from the exercise sessions?

Has it made you feel any different - in physical terms?

Has it made a difference to how you feel mentally, in terms of well-being?

Did the exercises affect the way you felt about yourself or saw yourself?

Has the way you have felt during your eight weeks of exercise affected any other part of your life?

Sleep patterns, coping, concentration, relaxation, relationship with others?

What do other people think about you exercising?

Did doing the exercises affect your relationships with other people?

What kept you coming here?

After the study

How have your expectations and perceptions about exercise changed from before you started the exercises to now, when you have just completed eight weeks of regular exercise?

Have you learnt anything new about yourself over the course of the study?

Do you think you will be able to carry on exercising now you have completed your exercise sessions here?

Do you foresee any problems that might get in the way of you keeping up some exercise participation?

Do you think what you have experienced and felt over the last eight weeks will be a sufficiently strong motivator to keep you active in the future?

What would be your biggest incentive or motivation to keep exercising?

What would help you to sustain your exercise participation?

Would you like someone to help you in the future with your exercise participation? What role would they play?

Given your recent success in doing your exercises do you think you could have done similar exercises sooner after finishing your treatment?

What I'd like to do is ask you some questions about your exercise level prior to your diagnosis and treatment...

Yeah O.K.

So, prior to your diagnosis and treatment were you regularly physically active?

Er the only thing I did as often as possible was I used to walk "x" round to school, erm, I'd walk as much as possible

And do you remember what your thoughts and perceptions were about exercise prior to your diagnosis and treatment?

Yeah it was important but not like I see it now, because at that time I hadn't suffered from depression, I hadn't er so I just did it without thinking why and everything...

O.K. Did you feel as though you were doing enough exercise or did you feel like you could have done more?

I felt as though I could have done more but it's just that you get yourself into ruts regards exercise, you know we used to go cycling as a family and you know you get out of that and then it's difficult to get you motivated get you back into it

What I'd like to ask you now is about the period of time once you had started your treatment and moving onto when you finished your treatment, during your treatment did you ever think about exercise...was that something you might have been capable of?

My mind wanted to do it, my body wouldn't let it and I gave into that it was just too stressful, you know having the chemo it makes you feel so poorly all you want to do is go to bed

Were you feeling quite fatigued with the treatment?

Yes, yes I used to have a chemo on a Thursday and by Sunday, I was wiped out you know

Yes you didn't feel like you had any energy?

Gosh, no, I can't explain it's more than not having any energy it just wipes you out

Overwhelming?

Yes it is very much

At that point were your thoughts just about getting through treatment?

Yeah, I mean you just don't see the light at the end of the tunnel at that stage you think when's the next treatment, taking it stage by stage and looking towards your next chemo and mine was every three weeks, and my middle week and you looked for that week so you could do things with the family, because you know then you will be back to chemo.

Was there a point anywhere in that treatment phase where you thought well maybe now I feel like I could do exercise? or was it not until you finished and some way after?

It was actually some way after, during chemo no way, when I finished chemo I expected to be up and running and all sorts but it doesn't happen like that, your still feeling tired, again my mind was wanting to go, my legs were really heavy even when I walked "x" up to school

And that spilled over for a while did it?

Yeah, a long time, yeah

What I am going to ask you about now is sort of coming here to the centre and doing the exercise sessions, why did you choose to get involved in the study?

Because I always believe you have to do as much as possible to try and help you, yourself, and also doing research you know will help other people stuck down with cancer

You came and which condition were you allocated to?

The exercise

So you were doing three times a week, eight weeks, on the go type of activity

Yeah

Did you enjoy the sessions?

Yeah, loads (Laughs)

O.K. What did you like about them?

The exercise sessions itself, actually getting myself to them was a bit stressful once I was there erm, it just motivates you, it makes you feel buzzing, alive you know on like a few occasions I could have fallen asleep waiting for Sue and felt really tired but at the end of the session I felt wide awake, so it was good

Did you have apprehensions at the beginning? - you said about your legs being really heavy and tired, did you experience that at the beginning

I talked it through with Sue and we did stretching exercises at the end, you know and it was going on the treadmill at first I didn't find that too taxing, what I find really, really difficult was the exercises at the end I find that really hard going

Would that be more like the stretching exercises?

Yeah, yeah

O.K. you mentioned about getting here that was stressful, was there anything else you didn't really enjoy, or didn't like the way it was set up?

No, no, it was very supportive

And just thinking about the sessions were they as you expected they might be?...Did you have an idea that they might be more difficult, less difficult?

No it was good because we had got four pieces of equipment in there, quite relaxed as to which equipment, initially it was quite relaxed which equipment I went on and then as I got into other exercises, but Sue coaxed me onto the others which I was really anxious about, but gals I went on them because it was like a progression

Do you mind if I ask you about that anxiety, going on and doing other things?

No

Do you think, you know if you hadn't have had someone to push you a little bit would you maybe have not gone onto to those things?

I wouldn't have done it on them, no

And having done it how did you feel about it?

I feel more confidence about using that equipment, I mean everybody doesn't like to look silly do they? but now I would use that equipment again

So would you say you now feel confident in your own ability to exercise?

Yeah, its' amazing how the transformation in myself and I put it down mainly to the exercise giving me confidence

Are you able to expand on that a little bit for me, what the transformation has been or where it has happened?

I felt negative about myself, I was getting tired easily even going up the stairs was really effort, and the consequences of that are you get irritable you cant see, the future doesn't look as good, by coming here it's actually altered all that, you know I mean, I don't feel as tired, I can jog! (laughs) your outlook is more positive, the outlook it's more positive

Sure, sure, that's quite lot of mental change as well as physical...

Yeah, I've seen, I actually think the mental side of things is bigger, the positive it's greater than actually the physical, you know when you go through counselling and cancer it is psychological, medically yeah, you've had breast cancer have to have a lumpectomy or mastectomy and other treatment, psychologically it's huge you know and sometimes people miss the enormous impact psychologically and sometimes that doesn't always get addressed

Just because you can't see it?

Yes absolutely

So you've answered a lot of these questions along the way which is fantastic, what I would like to ask you now is ...does it affect how you see yourself now

I am more confident, I mean making decisions before I had a problem so in a positive way I am more confident in the decisions I make and in actually what I do regards about myself not so much but I think I had a reconstruction in June and that's not completed and when that is finished, you know when it's completed I will probably look, feel different then

Sure, that transformation that exercise has given you is that only lasts while your exercising is it like a dose response thing do you have to be exercising to get that?

Yes, absolutely

What about ...because this is a week after you have finished is it something that will last or do you think it will only last while you are exercising?

If I don't exercise within two or three days my mood will plummet and I will get quite frustrated, I need to exercise

O.K. do you think that is something that you could have done sooner, do you think you could have got these benefits sooner if you had exercise, had this sooner?

Yes, I do definitely I was diagnosed with cancer April, well, May 2004 and I finished treatment the end of August the same year, so probably the beginning of 2005

O.K. that's interesting because with this study we had to wait for everyone to be a year to take part, have any of the beneficial effects spilled over into family life does it extend that far?

Yeah, actually well, because like usually the Mum is the hub of the family aren't they? and people come to them and actually it was difficult because I was probably stressed when I got cancer and I had the kids coming to me and it was like WOOH!, but no, it's back to normal, my husband put weight on, but we got an exercise bike and he is on that everyday, so it's benefited everybody

O.K. are you surprised it spread that far?

Yeah, but if one member of the family is not functioning properly it will have that knock on effect

Is there anything else you have experienced that works like exercise? ...Whether it's talking to someone else, diet, listening to music?

I did do counselling, I went through a series of counselling sessions erm, but nothing has helped me as much as the exercise in fact it really surprised me to the extent of how I felt afterwards, after the exercises

Have you any idea why?

Do you mean medically?

Anything... it just seems quite a simple thing to do but why does it work, or what is it about it?

I don't know I think, I mean , I feel what can I say, heavy lethargic, and there not nice things, so it's not about losing weight, it's not about getting fit in that sense, it's just when you've gone on a bike ride or a walk you feel brighter in yourself, lighter

So it might be physical actions, movement and doing something to energise you, because you have had one to one guidance - is it useful to have someone to talk to about your experiences, your health as well as the exercise?

Unfortunately for "xxx" I off loaded quite often and at the end I thought um you know, ...it's nice having that one to one than rather in a group session,

And what would you say was the main thing that kept you coming, because you made all your sessions?

It's because it's altered me, I don't get the tiredness in my legs like I used to it's the benefits that I've got from it

O.K. you have finished your eight weeks of exercise; I think you have answered this about how your expectations and perceptions towards exercise have changed from before you started to now...

Yeah, It's like before you can't see the wood for the trees it's all muddled, whereas now I don't think about cancer as much, I have moved on when I first cancer it was like a big arrow (points at self) this woman has had cancer I hated that but I didn't know how to work through that, and doing the exercises or it's because of the length of time as well but yeah you do think about cancer but it won't take over yeah you've had cancer and what do you do now

Do you think you will carry on exercising?

Yeah of course

Do you have plans?

Well yeah, I mean I've got my bike, what I plan to do is at the weekend, well walk "x" to school anyway, walk as much as possible, and at weekends..., I do enjoy walking, I love mornings, probably get up and go on a walk before the kids get up

Do you foresee any problems that might stop you keeping up with your exercise participation?

Well yeah, because as a family we are quite busy, the kids are in bands, I'm quite often then taxi, my husband has got a job where he doesn't get in till late at night and also I'm on full time placement at the moment, so actually it's frustrating how to find the time, it's important to find the time but it's going to take a bit of working out

O.K. the things you have been telling me about, your experiences from over the last eight weeks do you think that is going to be a sufficiently strong motivator to keep you exercising?

Yes I do, so much has changed for me, so from then when I started at the centre to now the transformation in me is huge, so I will carry it on.

Given your recent success's doing what you've been doing at what point do you think you could have started sooner?

I finished chemo the end of August four months after finishing treatment because as regards breast cancer the operation is not huge, it's not really as though you are getting over the operation, they are taking something away so it's not that major, so physically yes even sooner it just depends how long your treatment is

Do you think there is anything else that would improve your quality of life?

You mean apart from not having cancer (laughs)

Is there anything else you can think of that may do a similar thing as exercise has done for you?

I can't think of anything that will have a major impact as exercising has done, I don't know probably if for me I could get for "me" time you know more time for me

Was that part of the exercise at all - that it was your time?

Possibly yes, I do miss, I miss, even if I'm in the house, the kids find you because wherever you are, apart from exercise some more me time, I did start doing that actually before, well just after treatment, going for Indian head massage, facials, which I'd never ever done that before and that was O.K. because it's not too intrusive

I don't have any more questions for you "x" are there any other comments you would like to make or points that you would like to make as regards what you have been through and exercising?

No, I think we've covered it did you only take ladies that were post a year?

Yes a year to three years post treatment, well thanks for going through that it was really interesting and I really appreciate you taking the time to do that; that concludes what we are doing today, thank you.