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Abstract

To test the effects of a low to moderate intensity exercise on fatigue and overall QOL, both physiologically and psychologically in women who completed breast cancer treatment. Methods: Twenty-two women, ages 43-79, who had completed treatment for breast cancer, were randomly assigned to an exercise (n= 12) or control group (n = 10). The exercise group participated in a low-moderate intensity (30-50% heart rate reserve) aerobic exercise program 3 times a week for ten weeks. The control group did not participate in the exercise program. Physical functioning was measured by assessing peak aerobic capacity with a treadmill protocol. Both groups recorded their weekly level of fatigue using the Schwartz Cancer Fatigue Scale (SCFS) and Linear Analogue Self-Assessment (LASA). Results: Peak aerobic capacity increased in the exercise group 32%, which was significant, between (p = .0012) and within (p = .005) in the groups. The control group showed a decrease of 4.8%. Body fat decreased significantly within the exercise group over time (p = .0001). Sit and reach increased significantly within the exercise group 10% over time (p = .004). Body mass index decreased in the exercise group and this difference neared significance within the exercise group over time (p = .06). Fatigue reported with the SCFS decreased 55% in the exercise group and increased in the control group. This change was statistically significant between the groups (p = .0003) and within the groups (p = .01). The decrease in depression in the exercise group (89%) neared significance (p = .052) and the difference between the two groups was significant (p = .04). Anxiety decreased significantly in the exercise group 86% (p = .03) and significantly different between the groups (p = .01). Confusion decreased significantly (p = .04) and anger decreased significantly (p = .02) between the exercise group compared to the control group. Energy increased 69% within the exercise group significantly (p = .0005). Conclusion: This aerobic exercise program was effective in improving aerobic capacity, lower-body flexibility, fatigue, depression, anxiety, confusion, anger, and energy in the exercise group of breast cancer survivors. Low to moderate intensity exercise produced positive health benefits both physiologically and psychologically and should be considered as a safe, well-tolerated, rehabilitative tool for breast cancer survivors.

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I would like to express sincere appreciation to the U.S. Army Medical Research and Material Command for this outstanding educational opportunity. The opportunity to undertake this research has truly enriched my life as well as the communities in North Central Washington State. Exercise programs, resource brochures, and medical conferences are now in place for cancer survivors. On a personnel note, I am also looking forward to completing my doctorate as this grant has provided the means to do so. Thank you for your support.

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I. INTRODUCTION

Specific Aims

A growing body of evidence suggests that cancer survivors who participate in an exercise program have substantially reduced cancer treatment-related symptoms. Cancer treatment-related fatigue is the most common complaint from cancer patients and has devastating effects. There are few published studies looking at the effects of physical activity on the reduction of fatigue for breast cancer survivors. We hypothesized that low to moderate (30-50% heart reserve) intensity aerobic exercise will improve fatigue, depression, anxiety, and increase aerobic capacity.

The specific aims of this study were to test the effect of low to moderate intensity aerobic exercise treatment on self-reported fatigue, depression, anxiety, and physical functioning in women who have completed therapy for breast cancer.

We hypothesized that women recovering from cancer therapy in the low to moderate exercise group:

1. Would increase aerobic capacity between the pre-treatment assessment and the assessment after 10 weeks and
2. Would decrease their self-reported fatigue, anxiety, and depression levels over the first 10 weeks of treatment compared to the control group.

II. BODY OF RESEARCH

A. Significance

Breast cancer has a profound impact on women's health. An estimated 211,240 women with invasive breast cancers were diagnosed in 2005. An additional 58,490 with breast cancer in situ were also diagnosed (American Cancer Society, 2006). The incidence of developing breast cancer is about 13% (1 in 8) by age 95 in the United States (DeVita, 2001).

Almost 9 million Americans are cancer survivors (Neiman, 2006). Cancer survival has increased steadily over the last 35 years for all cancers combined. An estimated 64% of those diagnosed with cancer can expect to be alive in 5-years compared to 1971 when long-term survival was estimated less than 50% (Demark-Wahnefried, 2005). As the numbers of survivors are increasing, so are the long-term health issues specific to cancer survivorship. This is rapidly leading to an emerging public health concern (Demark-Wahnefried). The most recent estimate for 5-year survival is now 62% across all cancers and all disease stages (Courneya, 2003). Common cancers, if detected early, such as breast, colon, and prostate now have a 90% survival rate (Courneya, 2003). Survivorship issues are becoming increasingly important, including: improving quality of life (QOL), decreasing the risk of cancer recurrence, and promoting longevity.

The American College of Sports Medicine (ACSM) recently published their 7th edition of guidelines for exercise testing and prescription and yet there are still no established guidelines for people wanting to exercise after cancer treatment (ACSM, 2006). Guidelines for an exercise intervention are in place, however, for other chronic diseases such as diabetes and cardiovascular disease. Sedentary cancer survivors may be at increased risk for developing other diseases such as diabetes and heart disease. Recent data also suggests that sedentary cancer survivors may be at increased risk for cancer recurrence compared to active cancer survivors (McTiernan, 2004).

Specific exercise prescription guidelines for cancer survivors have posed many challenges for the ACSM, as there are so many different types of cancer and different therapies for each type. The lack of information on the underlying mechanisms of the benefits of exercise precludes the prescription of a precise mode, frequency, intensity, and duration of exercise (Nieman, 2006). Little data exists on the optimal length of time and most efficacious exercise intervention for cancer survivors. The ACSM has indicated that in healthy populations, important health benefits are realized in 15-20 weeks of regular exercise with marked improvements starting at 6 weeks (Kenney, 2000).

Fatigue

Fatigue is by far the most common symptom reported in patients undergoing cancer treatment. Fatigue has been defined as complete lack of energy and severe mental exhaustion (Burnham, 2002). Fatigue, compared to all other side effects of cancer treatment has the most negative effect on quality of life and general well-being. More than 70% of patients receiving chemotherapy or

radiation reported fatigue symptoms including: tired legs, whole body tiredness, and feelings of wanting to lie down. Fatigue increases with the number of radiation or chemotherapy cycles. Fatigue is associated with many diseases including cardiovascular disease, diabetes, depression, and cancer. Fatigue can cause coping mechanisms to fail, which negatively impacts physical functioning and hinders role functioning at home and work.

Most breast cancer survivors go through a period of reduced activity after diagnosis and treatment. Women are significantly less physically active during the first year after diagnosis and treatment, and only 50% return to prediagnosis levels at 3 years (Irwin, 2005). What is not known is the extent to which fatigue contributes to a sedentary lifestyle or vice-versa.

The roll of exercise as a rehabilitative tool is now being investigated but the studies are still few in number. Clearly, more randomized trials are needed to validate the few and very significant studies of exercise, as an intervention, to promote physiological and psychological functioning, and particularly the influence on fatigue.

Summary

Research looking at the role of exercise as a rehabilitative tool for cancer survivors has only recently begun in earnest since the mid to late nineties (Courneya, 2003). Early research conducted in the eighties and on into the nineties mainly studied the effects of exercise during cancer treatment. During this time period, exercise may be considered more of a symptom management technique rather than as a rehabilitative tool. Trial designs were either observational or interventional, with more emphasis placed on physiological versus psychological outcomes.

With survival rates at 62 - 64%, long-term health issues specific to cancer survivorship are emerging as a public health concern. Survivorship issues have necessitated a major research effort in this field. The positive outcomes demonstrated in these studies support the need for second-generation studies directed at breast cancer survivors, which examine the type of exercise intervention, intensity, frequency, and optimal duration. This study attempted to help establish an exercise regimen that will assist breast cancer survivors in improving fatigue and their overall QOL, both physiologically and psychologically.

B. Methods

Subjects

Twenty-two women, ages 43-79, with breast cancer were recruited from Central and North Central Washington. North Central Washington is a rural area. Women had to drive up to 140 miles at the time of testing to participate. This study was part of a larger RCT, Burnham's "Exercise and the Effects on Quality of Life in Cancer Patients." Burnham's study looked at the effects of a supervised exercise program on quality of life and physical functioning in mixed population of breast, colon, and lung cancer survivors rehabilitating from cancer treatment.

To be included in this study the women were: a) 20-80 years of age, b) had stage I to III breast cancer, c) concluded treatment one to twelve months prior to enrolling, and d) were cleared to participate by their primary care provider. Women were excluded if they were being treated for other chronic diseases, which would contribute to their fatigue such as congestive heart failure and poorly controlled diabetes.

Recruitment was done through advertising in newspapers, radio interviews, posters, and word of mouth. Posters about the study were placed in local community centers, medical centers, clinics, and hospitals in both Central and North Central Washington State. Initial screening was conducted by phone interview. Each subject was informed both verbally and in writing as to the purpose and admission criteria of this study. Subjects who met admission criteria signed and received a copy of the informed consent.

Design and Procedures

At the first session, subjects were randomly assigned to either an exercise intervention group or usual care (control group) and demographics and baseline measures were obtained. Those assigned to the exercise group participated in a supervised low to moderate intensity (30-50 % heart rate reserve) exercise program 3 x week for 10 weeks. Baseline physical functioning was determined by measuring peak aerobic capacity (ml/kg/min) utilizing a walking treadmill protocol prior to randomization. They performed a second treadmill test 10-weeks after the initial treatment session. Women in both groups recorded their level of fatigue weekly using a Linear Analogue Self-Assessment Scale (LASA) and the Schwartz Cancer Fatigue Scale (SCFS). Participants were contacted by phone after the initial enrollment and between weeks 4-6 to check-in regarding how the program was going, answer questions, and promote compliance. Self-reported psychological measures were collected during the exercise program at week 5 and again at week 10 during the second treadmill testing.

Protocol for Exercise Intervention

The exercise intervention was a program designed specifically for breast cancer patients called the Lebed Method. Lebed-Davis developed a program using ROM exercises to help reduce lymphedema in breast cancer survivors (Sandel, 2005) with a focus on healing through movement and dance. The Lebed Method combines structured exercises with dance movements.

A total of eight women, 2 registered nurses, 2 exercise physiologists interns from Central Washington University, and 2 breast cancer survivors were certified in the Lebed Method. The 8 women trained together and implemented the same routines which were taught at each session. For this study, the exercise programs were held 3-days a week, for 10 weeks, in Yakima, Ellensburg, Wenatchee, and Brewster, Washington.

At the initial visit, heart rate reserve was calculated and each woman was given a Polar heart monitor and instructed in its use. All the women were taught how to calculate their own heart rate reserve, given their target range, and told to

exercise within the provided range ensuring that each participant exercised at 30-50% of their heart rate reserve.

The Karvonen method for calculating heart rate reserve (HRR) was used as follows:

$$\begin{aligned}\text{Maximum heart rate (MHR)} &= 220 - \text{person's age} \\ \text{Heart Rate Reserve (HRR)} &= \text{Maximum HR} - \text{resting HR} \\ 40\% \text{ HRR} &= (\text{HRR} \times .40) + \text{RHR}\end{aligned}$$

Example: age 50, resting HR 75, at 40% HRR.

$$\begin{aligned}220 - 50 &= 170 \text{ (MHR)} \\ 170 - 75 &= 95 \text{ (HRR)} \\ (95 \times .40) + 75 &= 113 \text{ at 40\% HRR}\end{aligned}$$

The HRR was calculated to provide the target heart range during the exercise intervention.

During each exercise session, the women spent the first 10-15 minutes doing aerobic warm-up exercises and stretching, which included head and neck stretches, arm circles, shoulder rotations, side-to-side arm extensions, and full-body contractions and extensions. This particular part of the exercise intervention helped facilitate lymphatic drainage and aided with lymphedema. The following 25-30 minutes incorporated low to moderate aerobic dance exercise (30-50% heart rate reserve). The dance movements were simple and no previous experience was necessary. Women became familiar with the workout music and routines. Upper body and extremity movements were performed to music with at least 4-6 repetitions each side. Stretch bands were also used to aid with resistance training. Lower body and extremity movements included side-to-side hip swings, dance steps utilizing forward and backwards flexion, extension, abduction, and adduction. This was followed by an aerobic cool-down (3-5 minutes) and stretching (7-10 minutes) for a total of 50-60 minutes per session.

C. Measures

Demographics

Demographics, Health History, Cancer, and Exercise characteristics were determined (see appendix A and B). Questions included their previous medical history, medications, and current symptoms. Cancer characteristics included a short history of the onset of cancer, assessment, and treatment. Exercise characteristics included current and past exercise programs, frequency of exercise, duration, and preferences.

Physical Function

Physical functioning was determined by measuring aerobic capacity during treadmill testing. Subjects established a comfortable walking pace of 1.5 to 4 mph. The grade of the treadmill was increased 1% each minute and continued until the subjects reported volitional exhaustion. Heart rate was monitored during treadmill testing using a Polar heart rate monitor (Target model). Oxygen consumption was measured using an open circuit indirect calorimetry technique. The metabolic cart was calibrated to known

concentrations of oxygen and carbon dioxide prior to each test. The subjects breathed into a 2-way valve system during the test, which is connected to the metabolic cart for analysis. The subjects inhaled room air while their exhaled gases go directly into the metabolic cart. This process permitted quantification of expiratory volumes, O₂ concentrations, and carbon dioxide concentrations and the calculation of aerobic capacity (mL.kg⁻¹.min⁻¹).

Lower-body flexibility was measured using a modified sit-and-reach test (Hoeger, 1992) as described by the American College of Sports Medicine (2006).

Anthropometric

Body mass index (BMI) was calculated by dividing body weight in kilograms by height in meters squared (kg.m⁻²). The percent of body fat was calculated as the sum of 3 skinfold measurements in mm. Skinfold measurements were taken using Lange calipers following procedures by Jackson and Pollock (1978) and the American College of Sports Medicine (ACSM, 2006). The sites measured on women were their triceps, suprailiac, and thigh. The standard error of the estimate is reported at $\pm 3.6\%$.

Psychological Distress and Fatigue

A modified Linear Analogue Self-Assessment Scale (LASA) and the Schwartz Cancer Fatigue Scale (SCFS) measured self-reported fatigue levels. The LASA was derived from the Profile of Moods States (POMS). It includes 6 scales: fatigue, depression, anxiety, confusion, anger, and energy. The LASA used a 100 mm line, that is anchored by the terms “not at all fatigued” and “extremely fatigued;” for energy levels “not at all energetic” and “extremely energetic.” The score is determined by measuring the placement of the mark on the line. Scores range from 0 to 100. Test-retest reliability of the scale 12 weeks apart in 60 cancer patients was $r = .61$ (Sutherland, 1988). Validity was based on the correlation with the original POMS, with the correlation $r = .79$.

The SCFS is a 6-item Likert scale which asks participants to rate the terms: tired, difficulty thinking, overcome, worn out, and listless as 1 “not at all,” 2 “a little,” 3 “moderately,” 4 “quite a bit” and 5 “extremely.” The SCFS demonstrated strong internal consistency reliability exceeding Cronbach alpha $> .85$ (Schwartz, 2002).

Statistical Analysis

Demographic data was measured by descriptive statistics (means and standard deviation). Aerobic capacity data was analyzed using a paired t-test. A two-way repeated measures ANOVA was used to determine if the changes to the self-reported fatigue and emotional distress levels were statistically significant. All values were reported as means and standard deviations. An alpha level of <0.05 was considered statistically significant. All analyses were conducted on StatView SE+ Abacus Concepts Inc. software.

D. Results

Subjects' Characteristics

The mean age of subjects in the control group was 55 (± 8.4 SD) and the exercise groups' mean age was 62 (± 9.6 SD). The majority of women were diagnosed with stage II breast cancer. The control group had two women with Stage I breast cancer and Stage III respectively. The exercise group had four women with Stage I and one with Stage III disease. The control group had seven women who were estrogen receptor positive and three negative. The exercise group had nine women estrogen receptor positive and three negative. See Table 1 for demographic data and past medical history.

As shown in Table 1, the subjects in both groups all had standard treatment for breast cancer. The control group had 10 women treated by lumpectomy, followed by chemotherapy with doxorubicin, cyclophosphamide ($N = 2$), and paclitaxel ($N = 2$). One participant was treated with cyclophosphamide, methotrexate, and fluorouracil and one was treated only with the aromatase inhibitor, anastrozole. Nine out of the 10 women received radiation therapy. The exercise group had 2 women treated with mastectomy. The other 10 women were treated with lumpectomy, followed by chemotherapy with doxorubicin, cyclophosphamide (5 participants), plus paclitaxel (5 participants). Ten of the exercise group had radiation therapy. The control group had 7 women on hormonal blockade with either tamoxifen or an aromatase inhibitor while the exercise group had 9 women.

The control group had 6 sedentary women, 1 who exercised irregularly, and 3 who exercised regularly. The exercise group had 6 sedentary women, 3 who exercised irregularly, and 3 who exercised regularly. No significant differences found between the groups for age, stage of their disease, hormone receptor status, treatment, exercise habits, or past medical history.

No subjects withdrew from either the control or exercise group. All subjects completed the ten-week study session and follow up measures. Over the 10 weekly exercise sessions the attendance rate averaged 94%. The exercise group had no reported problems or injuries.

Physiological measures

A repeated measures ANOVA showed peak aerobic capacity increased the exercise group by 31.5% (16.5 ± 8.1 to 21.7 ± 9.4). The control group, in comparison, showed a decrease in aerobic capacity of 4.8% (16.6 ± 5.1 to 15.8 ± 3.8). This change was statistically significantly between the groups ($p = .0012$) and within the exercise group over time ($p = .005$). See Table 2.

Body mass index (BMI) decreased in the exercise group (26.5 ± 4.1 to 26.2 ± 4.2). This change was not statistically significant between the groups but neared significance within the exercise group over time ($p = .06$).

Body fat percentage decreased in the exercise group by 4.7% (29.8 ± 3.7 to 28.4 ± 3.8). The change was statistically significantly within the exercise group over time ($p = .0001$).

Flexibility as measured by the sit and reach increased in the exercise group by 10% (30.9 ± 7.2 to 34.0 ± 4.9). This change was statistically significantly within the exercise group over time ($p = .004$).

Psychological self-reported measures

Results for psychological measures are listed in Table 3 and the weekly measurements are found in the appendices. Fatigue reported with the Schwartz Cancer Fatigue Scale (SCFS) decreased by 55% in the exercise group (17.8 ± 5.9 to 8.01 ± 3). Fatigue increased in the control group (11.8 ± 4.9 to 15.5 ± 8.3). This change was statistically significant between the groups ($p = .0003$) and within the groups ($p = .01$). Fatigue reported with the LASA scale decreased in the exercise group and increased slightly in the control group but the differences were not statistically significant between ($p = .17$) or within ($p = .10$) the groups.

Depression reported with the LASA scale decreased the exercise group by 89% (23.0 ± 19.0 to 2.5 ± 4.0). Depression increased by 73% in the control group (7.6 ± 8.1 to 13.2 ± 19.5). This change was statistically significantly between the groups ($p = .005$) and neared significance across time within the groups ($p = .052$).

Anxiety reported with the LASA scale decreased in the exercise group by 86% (31.6 ± 26.2 to 4.3 ± 5.7). This change was statistically significantly between the groups ($p = .03$) and within the groups over time ($p = .01$).

Confusion reported with the LASA scale decreased in the exercise group by 70% (21.0 ± 17.9 to 6.3 ± 14.1). Confusion increased by 60% in the control group (6.7 ± 6.6 to 10.7 ± 19.8). This change was statistically significantly between the groups ($p = .04$).

Anger reported with the LASA scale decreased in the exercise group by 71% (14.3 ± 21.5 to 4.1 ± 8.8). Anger increased over 200% in the control group (4.5 ± 4.7 to 13.8 ± 23.4). This change was statistically significantly between the groups ($p = .02$).

Lack of energy reported by the LASA scale improved in the exercise group by 69%. (70.2 ± 19.3 to 21.9 ± 30.0). This change was significant over time ($p = .0005$).

Table 1. Subject Characteristics (mean $\pm$ SD)

<i>n</i> = 22	Control (<i>n</i> = 10)	Exercise (<i>n</i> = 12)
Stage I	2	4
Stage II	6	7
Stage III	2	1
ER+	7	9
ER-	3	3
Type of treatment*		
Surgery	10	10
Lumpectomy	0	2
Mastectomy		
Chemotherapy		
AC	2	5
AC+Taxol	5	5
CMF	1	0
AI only	1	0
Radiation	9	10
Taking TAM or AI	7	9
Exercise		
Sedentary	6	6
Irregular	1	3
Daily	3	3
PMH*		
Unremarkable	3	2
Hypothyroid	3	6
HTN	3	3
DM	1	1
Hyperlipidemia	3	3
Osteoarthritis	3	2
SLE	1	0
COPD	0	1
Asthma	0	0

* Numbers may be greater or less than *n* due to combination therapy and diseases.

Abbreviations: ER, estrogen receptor, AC, Adriamycin, Cytoxan, CMF, Cytoxan, Methotrexate, 5FU, TAM, Tamoxifen, AI, Aromatase Inhibitor, PMH, past medical history, HTN, hypertension, DM, diabetes mellitus, SLE, lupus, COPD, chronic obstructive pulmonary disease.

Table 2. Physiological Measures (mean $\pm$ SD)

Dependent Variables	Pre-treatment	Post-treatment	% Change Pre - Post Treatment	P Values	
				AB	RM
Aerobic capacity (mL.kg ⁻¹ .min ⁻¹)					
Control	16.6 ($\pm$ 5.1)	15.8 ($\pm$ 3.8)	4.8%		
Exercise	16.5 ($\pm$ 8.1)	21.7 ($\pm$ 9.4)	-31.5%	.0012 ^t	.005*
BMI					
Control	30.1 ($\pm$ 5.8)	30.0 ($\pm$ 5.7)	.3%		
Exercise	26.5 ($\pm$ 4.1)	26.2 ($\pm$ 4.2)	1.1%	.19	.06
Body fat %					
Control	33.4 ($\pm$ 5.3)	31.8 ($\pm$ 5.1)	4.8%		
Exercise	29.8 ($\pm$ 3.7)	28.4 ($\pm$ 3.8)	4.7%	.61	.0001*
Sit and reach(mm)					
Control	28.5 ($\pm$ 9.7)	30.7 ($\pm$ 7.3)	-7.7%		
Exercise	30.9 ($\pm$ 7.2)	34.0 ($\pm$ 4.9)	-10 %	.60	.004*

* Significant within (RM) group difference over time, $P < 0.05$.

^t Significant between (AB) group difference, $P < 0.05$.

% Change = pre-post value/pre-value x 100

Abbreviations: SD, standard deviation, ml, milliliters, kg, kilograms, %, percent, BMI, body mass index, cm, centimeters,

Table 3. Psychological Measures (mean $\pm$ SD)

Dependent Variables	Pre-treatment	Post-treatment	% Change Pre to Post Treatment	P Values AB RM
SCFS Control Exercise	11.8 ($\pm$ 4.9) 17.8 ($\pm$ 5.9)	15.6 ($\pm$ 8.3) 8.1 ($\pm$ 3.4)	-32.2% 54.5%	.0003 ^t .01 *
LASA Fatigue Control Exercise	31.30 ($\pm$ 15.9) 41.0 ($\pm$ 23.0)	31.33($\pm$ 34.6) 19.4 ($\pm$ 29.9)	-0.09% 52.7%	.10 .17
Depression Control Exercise	7.6 ($\pm$ 8.1) 23. ($\pm$ 19.0)	13.2 ($\pm$ 19.5) 2.5 ($\pm$ 4.0)	-73% 89%	.005 ^t .052
Anxiety Control Exercise	16.3 ($\pm$ 19.7) 31.6 ($\pm$ 26.2)	15.9 ($\pm$ 21.6) 4.3 ($\pm$ 5.7)	2.5% 86.4%	.03 ^t .01 *
Confusion Control Exercise	6.7 ($\pm$ 6.6) 21. ($\pm$ 17.9)	10.7 ($\pm$ 19.8) 6.3 ($\pm$ 14.1)	-59.7% 70%	.04 ^t .1
Anger Control Exercise	4.5 ($\pm$ 4.7) 14.3 ($\pm$ 21.5)	13.8 ($\pm$ 23.4) 4.1 ($\pm$ 8.8)	-206.7% 71.3%	.02 ^t .7
Lack of Energy Control Exercise	53.2 ($\pm$ 18.9) 70.2 ($\pm$ 19.3)	33.2 ($\pm$ 28.9) 21.9 ($\pm$ 30.0)	37.6% 68.8%	.17 .0005 *

* Significant within (RM) group difference over time, $P < 0.05$.

^t Significant between (AB) group difference, $P < 0.05$.

% Change = pre-post value/pre-value $\times$ 100

Abbreviations: SD, standard deviation, SCFS, Schwartz Cancer Fatigue Scale, LASA, Linear Analog Self-Assessment.

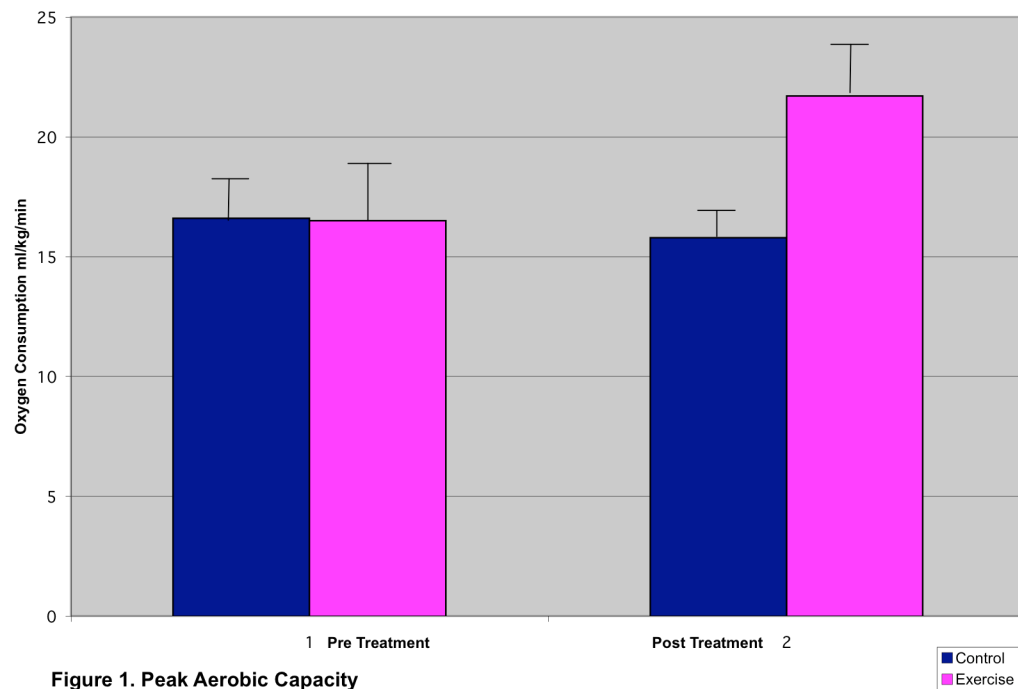


Figure 1. Peak Aerobic Capacity

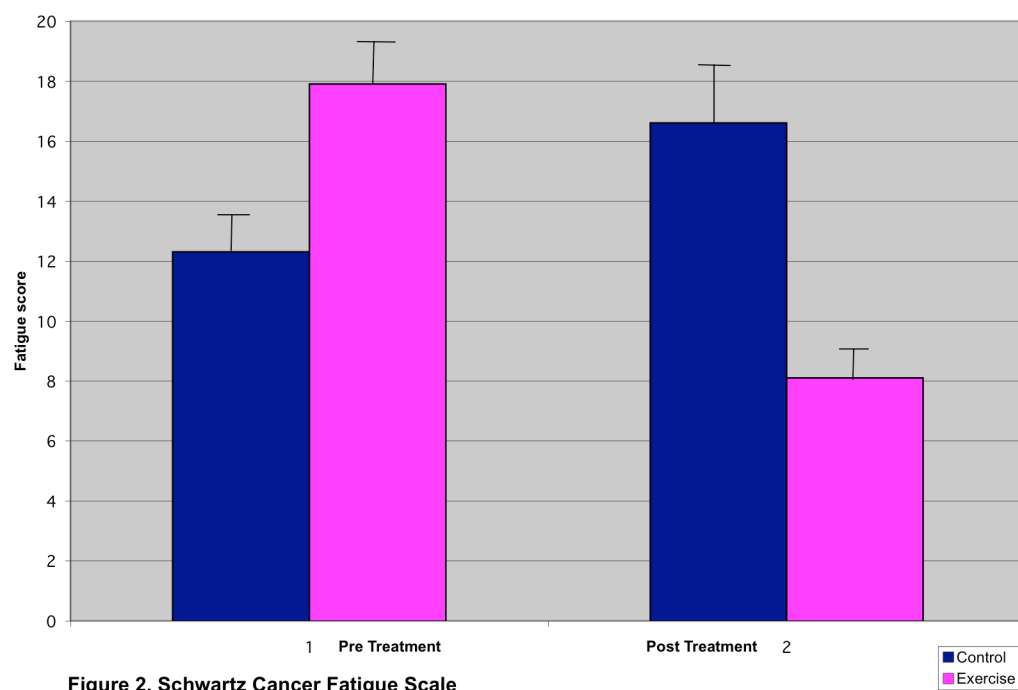


Figure 2. Schwartz Cancer Fatigue Scale

E. Discussion

Many women are now surviving breast cancer thanks to advances in early detection and treatment options. As the proportion of long-term breast cancer survivors continue to grow, so do the long-term health issues associated with the cancer diagnosis and treatment. Survivorship issues are quickly becoming a public health concern. Cancer survivors are at a greater risk for developing secondary cancers and other diseases brought on by cancer treatment, genetic predisposition, and lifestyle factors. Cancer survivors are increasingly seeking information, counsel, and guidance to ensure a healthier life and perhaps longer one as well, (Denmark-Wahnefried, 2005). Epidemiologic studies have consistently demonstrated the benefits of low to moderate regular exercise to promote health and reduce morbidity (Schwartz, 2001). More research is needed for the development of guidelines, exercise prescriptions, and other rehabilitative tools for this rapidly growing population.

Cancer survivors often experience long periods of inactivity while going through cancer treatment. Inactivity leads to a progressive decline in aerobic capacity and results in decreased physical functioning. This greatly impacts the ability to perform activities of daily living. Health care providers frequently promote rest and recuperation to reduce side effects of cancer treatment. Fewer than 4% of them encourage cancer survivors to begin or continue an exercise program (Schwartz, 2004).

The purpose of this investigation was to examine the effects of a low to moderate exercise intervention on fatigue and overall QOL, both physiologically and psychologically in women who have completed breast cancer treatment. There is little research determining the optimum mode, frequency, intensity, and duration of exercise required for beneficial effects in this population. There is also little research comparing supervised exercise programs to home-based ones (Stevenson, 2004). Recent trends in exercise programs encourage modest levels of physical activity to achieve health benefits.

This study found that a low to moderate exercise program significantly improved physiological measures of peak aerobic capacity, body composition, and lower-body flexibility. These findings were similar to that of Burnham and Wilcox (2002) who found that exercising cancer survivors increased psychological functioning and improved overall quality of life, decreased fatigue and anxiety, and increased energy. Their low and moderate intensity aerobic exercise program over 10-weeks was effective in significantly improving aerobic capacity, decreasing body fat, and improving lower-body flexibility. Courneya (2003) has conducted several similar trials showing consistent significant improvements in aerobic capacity with measures of peak oxygen consumption. Dimeo (1997) and Pinto (2003) also had similar findings though their exercise programs that incorporated a moderate to high intensity aerobic exercise program. Most interventional studies have been 12-weeks or less. This study showed statistically significant benefits after a 10-week exercise program. It's unknown whether the outcomes would have continued to show increased health benefits beyond 10-12 weeks duration.

This aerobic exercise program also significantly reduced psychological measures of fatigue (SCFS), depression, anxiety, confusion, and anger in this group of breast cancer survivors and increased their energy levels. These findings are consistent with other interventional studies with breast and mixed groups of cancer survivors. In the Rehabilitation Exercise for Health after Breast Cancer (REHAB) trial, Courneya et al. (2003), found significant decrease in fatigue, self-esteem, and over-all QOL. Courneya (2003) also found significant improvements in fatigue, improved functional well-being, and satisfaction with life in the Group Therapy and Home-Based Physical Exercise (GROUP-HOPE) trial. Segar et al (1998) had significantly decreased depression and anxiety in their exercise group compared to the control group. These studies, including, Porock (Galvao, 2005) and Sandel (2005), represent a consistent trend in positive adaptations with exercise.

Fatigue decreased significantly both between the groups and within the groups as measured with the Schwartz Cancer Fatigue Scale (SCFS). Fatigue measured by the LASA showed the same “trend” though it did not reach statistical significance partially due to the small sample. Increasing the numbers of subjects may also have increased the power of this analysis. The LASA scale may not be sensitive as the SCFS for measuring fatigue as it is a single item where the SCFS is a six-item scale. Increasing the numbers of subjects may also have increased the power of this analysis.

Adherence

The exercise program utilized in this study was well tolerated by the participants. The adherence rates for attendance were also very high, averaging about 94%. This notably high adherence rate is consistent with other studies performed after completion of cancer treatment (Oldervoll, 2004). This may reflect a select group of cancer survivors who are interested in participating in a rehabilitative program after cancer treatment. Future studies should look at characteristics of the cancer survivors who decline to participate such as age, education, health habits, and level of fitness, body mass index, and mood.

Exercise programs for cancer survivors are often limited by the symptoms and residual side effects they experience from cancer treatment. The low to moderate intensity exercise intervention in this study did not exacerbate any symptoms we measured. The lower intensity levels may have allowed the participants to adapt more easily to exercise, which may be the reason the exercise sessions were well attended compared to other studies which used higher intensities. None of the participants withdrew or were injured which indicates that this population can exercise safely and effectively for extended periods of time.

The women who participated in this study were highly motivated. Greater than 50% who participated were sedentary women and did not exercise at all. The exercise intervention utilized in this study was a structured, supervised program, which guided them through a progressive exercise program specifically

developed for breast cancer survivors (reduce lymphedema and increase range of motion). This may have also have promoted self-efficacy in addition to improved adherence in sedentary individuals.

A benefit that was noted was the development of a support system for the participants. None of the women were in support groups nor had any interest in joining such a group. The design of using a supervised exercise intervention became a major benefit as the women gained tremendous support from each other. This is consistent with other studies (Turner, 2004).

Strengths and Limitations

Limitations to this study include the small number of participants thus making it difficult to generalize the findings to larger and more varied populations of cancer survivors. More studies are needed with larger populations to evaluate the effectiveness of low to moderate exercise programs. The participants who volunteered may have been a healthier population thus making it difficult to generalize to other populations. Also, the sample was predominately Caucasian, further limiting generalizability as noted in similar studies (Schwartz, 2001). More subjects may have increased the statistical power of our analysis.

Strengths include that the sample was matched in regards to the stage of breast cancer and treatment. It was a randomized controlled trial. The control group was offered the exercise intervention when they completed the study so there was no demoralization, which may have affected the bias of the participants.

III. KEY RESEARCH ACCOMPLISHMENTS

Key Findings

- Fatigue reported with the SCFS decreased 55% in the exercise group and increased in the control group. This change was statistically significant between the groups ($p = .0003$) and within the groups ($p = .01$).
- Peak aerobic capacity increased in the exercise group 32%, which was significant, between ($p = .0012$) and within ($p = .005$) in the groups. The control group showed a decrease of 4.8%.
- Body fat decreased significantly within the exercise group over time ($p = .0001$).
- Sit and reach increased significantly within the exercise group 10% over time ($p = .004$).
- Body mass index decreased in the exercise group and this difference neared significance within the exercise group over time ($p = .06$).
- Depression decreased in the exercise group (89%) and neared significance ($p = .052$) The difference between the two groups was significant ($p = .04$).
- Anxiety decreased significantly in the exercise group 86% ($p = .03$) and significantly different between the groups ($p = .01$).
- Confusion decreased significantly ($p = .04$).
- Anger decreased significantly ($p = .02$) between the exercise group compared to the control group.
- Energy increased 69% within the exercise group significantly ($p = .0005$).

IV. REPORTABLE OUTCOMES

Degree/Licensure Obtained: Master of Nursing, University of Washington
ARNP, Washington State.

Conference: *Current Issues in Cancer for the Primary Care Provider* (2005).

Publications:

- Kemble, K., Burnham, T. (2006). *Aerobic exercise decreases depression and anxiety in breast cancer survivors*. *Medicine and Science in Sports and Exercise*, Volume 38:5 Supplement.
- Burnham T., Nethery V., Frank J., Kemble K., (2005). *Relationship between fatigue and measures of emotional distress in exercising cancer survivors*. *Medicine and Science in Sports and Exercise*. 37:5, 2005.
- Frank, J., Burnham T., Kemble K., (2005). *Low-moderate intensity aerobic exercise improves quality of life indices and emotional distress in cancer survivors*. *Medicine and Science in Sports and Exercise*. 37:5, 2005.
- Sims C., Burnham T., D'Acquisto L., Papadopoulos C., Kemble K., (2005). *Low intensity aerobic exercise improves quality of life and body composition in breast cancer survivors*. *Medicine and Science in Sports and Exercise*. 37:5, 2005.

Presentations:

- Poster titled *Aerobic Exercise Decreases Depression and Anxiety in Breast Cancer Survivors*. 53rd Annual Meeting of the American College of Sports Medicine, Denver, CO, June 1-4, 2006.
- Presenter for poster and platform presentation titled *The Effects of Low to Moderate Intensity Aerobic Exercise on Fatigue in Breast Cancer Patients Following Clinical Treatment* at The Era of Hope, DOD Breast Cancer Research Program, Philadelphia, PA. June 8-11, 2005.
- Co-presenter with T. Burnham on paper titled *Relationship Between Fatigue and Measures of Emotional Distress in Exercising Cancer Survivors* at the annual meeting of the American College of Sports Medicine in Nashville, TN. June 1-4, 2005.
- Co-presenter with J. Frank on paper titled *Low-Moderate Intensity Aerobic Exercise Improves Quality of Life Indices and Emotional Distress in Cancer Survivors* at the annual meeting of the American College of Sports Medicine in Nashville, June 1-4, 2005.
- Co-presenter with C. Sims on paper titled *Low Intensity Aerobic Exercise Improves Quality of Life and Body Composition in Breast Cancer Survivors* at the annual meeting of the American College of Sports Medicine in Nashville, TN. June 1-4, 2005.

Honors

- 2004 Honorary Alumni, Wenatchee Valley College, Wenatchee, WA.
- 2005 Sigma Theta Tau International, Honor Society of Nursing.
- 2006 Nominee, Humanitarian Award, Biobehavioral Nursing & Health Systems, UW.

V. CONCLUSION

Summary

Prescription guidelines for an exercise intervention are already in place for chronic diseases such as diabetes and cardiovascular disease but no guidelines are in place for cancer survivors though aerobic exercise recommendations are now being suggested by the American Academy of Sports Medicine. Determining the optimal exercise prescription for the individual patient recovering from therapy is a large challenge awaiting future research (Neiman, 2006). Low to moderate intensity aerobic exercise should be considered for this population.

This study, consistent with several other studies, found that low to moderate intensity exercise produced positive health benefits both physiologically and psychologically. Exercise prescriptions, as in this study and others, should be utilized and encouraged for this population as a rehabilitative tool by health care providers.

The physiological improvements noted in this study may be responsible for the positive psychological effects women experienced. Improved aerobic capacity increased physical functioning, which is important in reducing fatigue and improving quality of life in cancer survivors. This study demonstrated that a low to moderate exercise program helps reduce post-treatment related fatigue and emotional distress while improving physical functioning in breast cancer survivors.

VI. BIBLIOGRAPHY

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Kemble, K., Burnham, T., Gallucci, B. (2005). *The effects of low to moderate Intensity exercise on breast cancer patients following clinical treatment*. Era of Hope, Philadelphia.

Kemble, K., Gallucci, B., Belsa, B. (2006). *Low to moderate aerobic exercise improves fatigue, depression, anxiety, and aerobic capacity in breast cancer survivors*. Thesis submitted to UW.

Personnel

Katherine Kemble, MN, ARNP
Tim Burnham, PhD, Consultant

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VII. APPENDICES

Appendix A

Medical History Questionnaire

Name:

1. Describe the type and stage of the cancer you are experiencing.

2. What type(s) of therapies were you receiving?

3. Are you experiencing any symptoms from your treatment? If so please list these symptoms (i.e. fatigue, nausea, brittle bones etc.)

4. Do you have any other health problems that may be aggravated by physical activity? If so please list these problems (i.e. cardiovascular disease, diabetes, respiratory problems etc.)

5. Are you currently on any medications? If so please list them.

Appendix B

Exercise History

- 1.** Are you currently participating in any sort of physical activity? If so, what type? If the answer to this question is no, please skip to question 4.

- 2.** How often (how many times per week) do you participate in an exercise program?

- 3.** In each individual exercise session how long do you exercise?

- 4.** Describe your exercise history to me. In other words, tell me about your past exercise experiences. This can be things like sports teams, walking programs, weight lifting, aerobics etc. If you have not exercised in a number of years, that's fine. Tell me what you liked to do for exercise as a teenager or even a child.

- 5.** What do you dislike about exercising?

Appendix C

Schwartz Cancer Fatigue Scale- 6-Item (SCFS-6)

The words and phrases below describe different feelings people associate with fatigue. Please read each item and circle the number that indicates how much fatigue has made you feel in the past **2 to 3 days**.

1 = not at all

2 = a little

3 = moderately

4 = quite a bit

5 = extremely

Tired	1	2	3	4	5
Difficulty thinking	1	2	3	4	5
Overcome.....	1	2	3	4	5
Listless	1	2	3	4	5
Worn out	1	2	3	4	5
Helpless	1	2	3	4	5

Appendix D

Linear Analogue Self-Assessment Scale (LASA)

Developed by: Heather J. Sutherland, Patricia Walker, and James E. Till

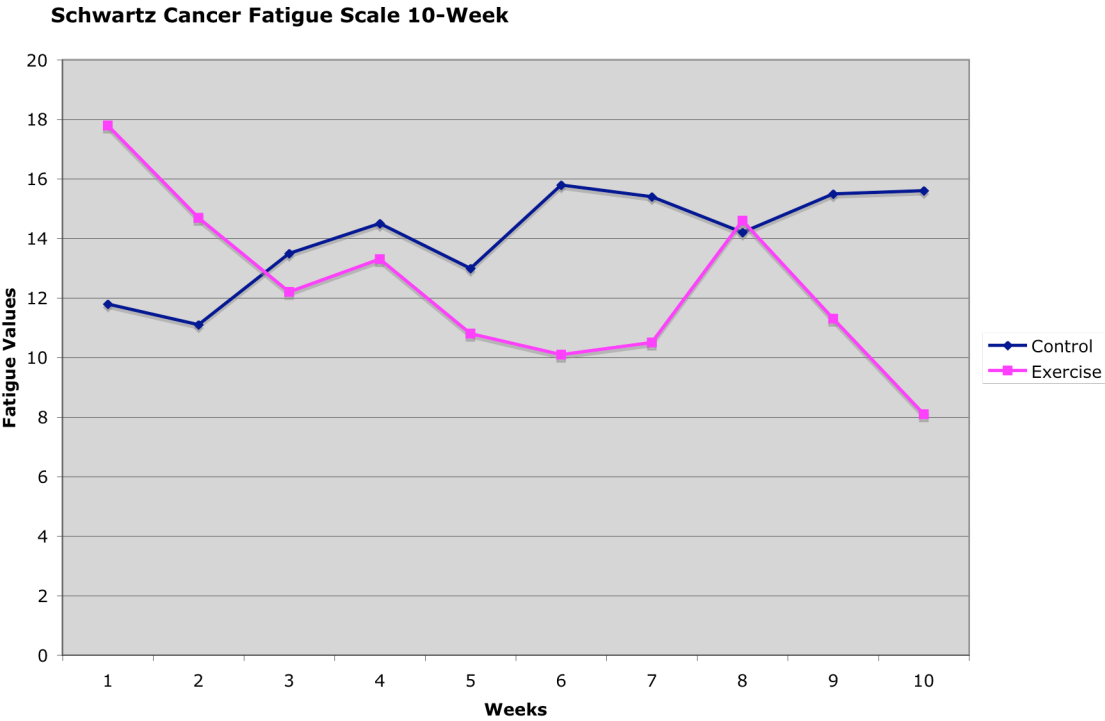
Instructions: Place a vertical mark on each scale at the position that best describes your state during the last week.

How have you been feeling during the past week?

- | | | |
|----------------------------|-------|------------------------|
| 1. Not at all
fatigued | _____ | Extremely
fatigued |
| 2. Not at all
anxious | _____ | Extremely
anxious |
| 3. Not at all
confused | _____ | Extremely
confused |
| 4. Not at all
depressed | _____ | Extremely
depressed |
| 5. Not at all
energetic | _____ | Extremely
energetic |
| 6. Not at all
angry | _____ | Extremely
angry |

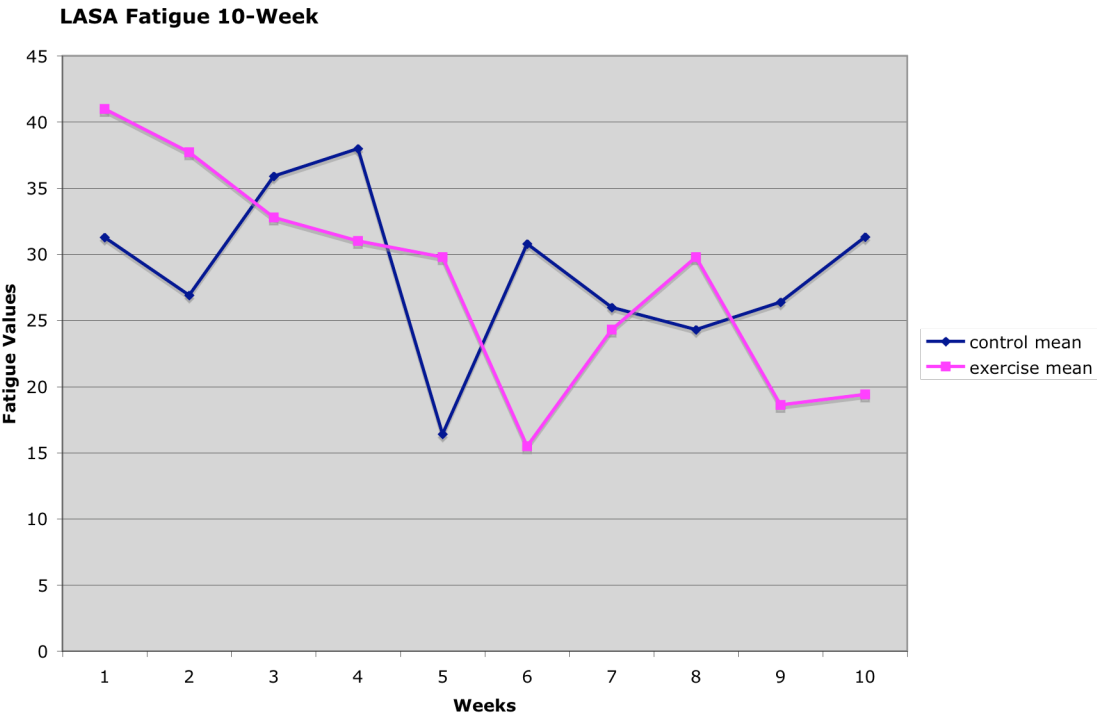
Appendix E

Schwartz Cancer Fatigue Scale 10-Weeks



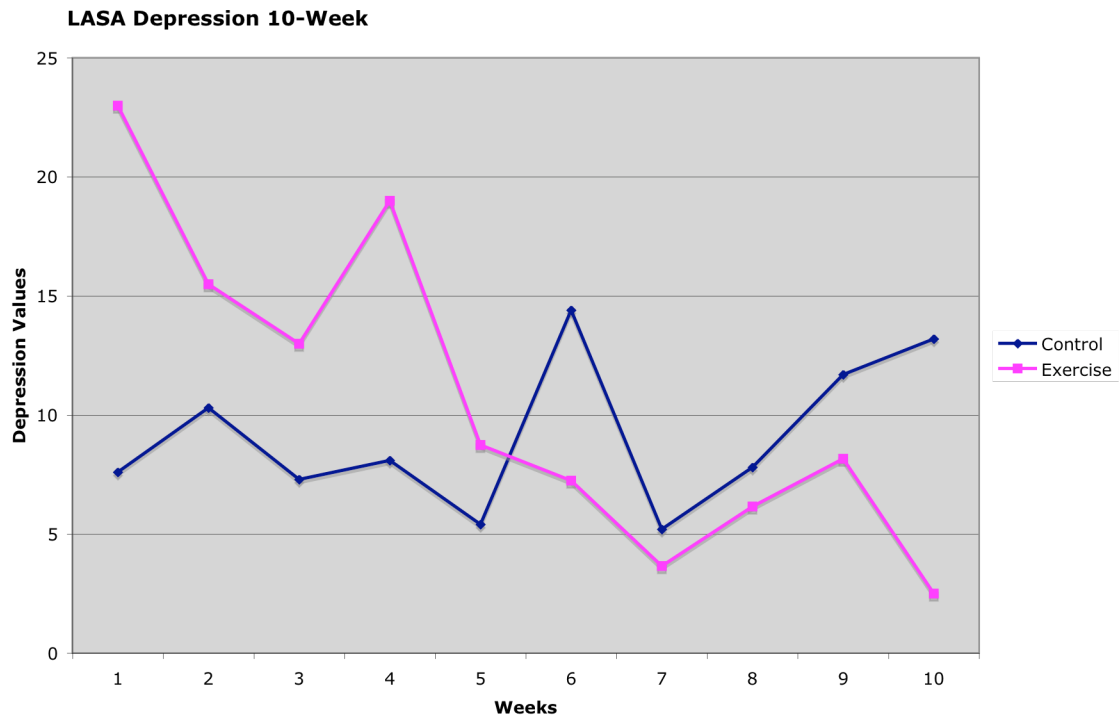
Appendix F

LASA Fatigue Scale10-Weeks



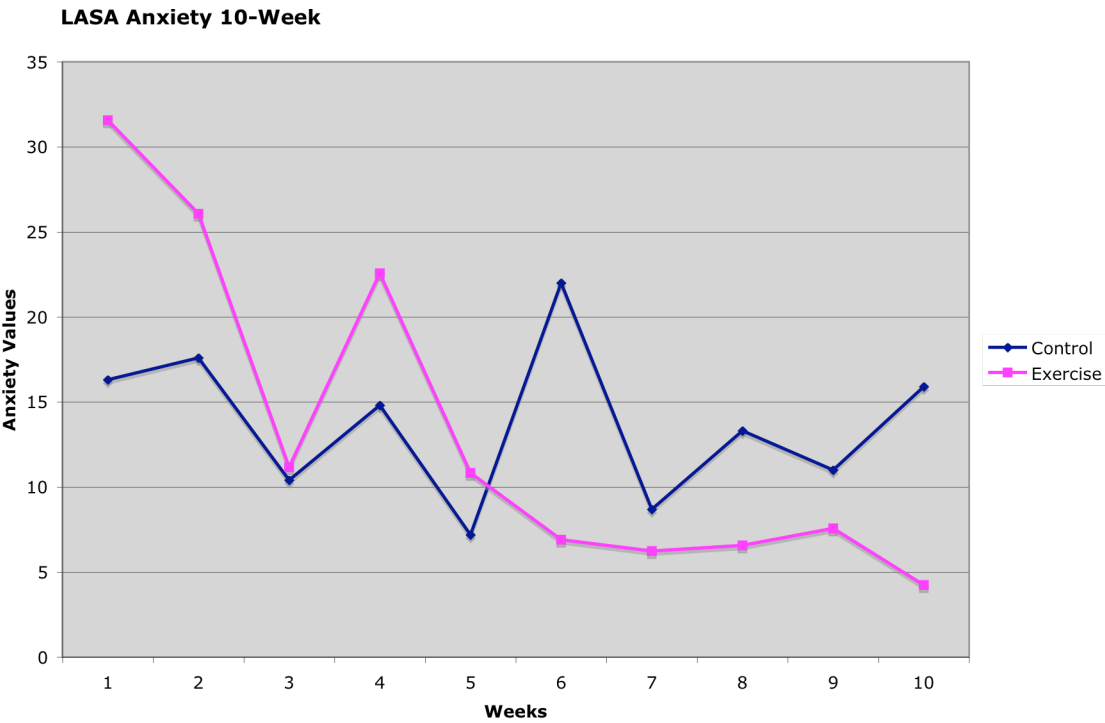
Appendix G

LASA Depression Scale 10-Weeks



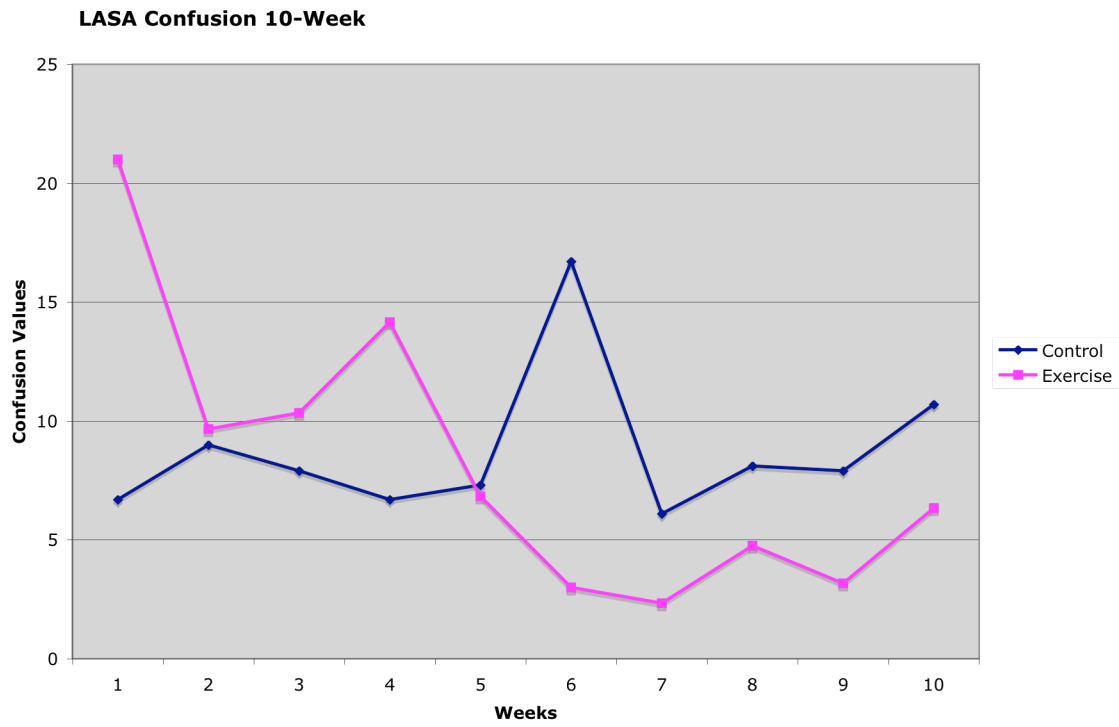
Appendix H

LASA Anxiety Scale 10-Weeks



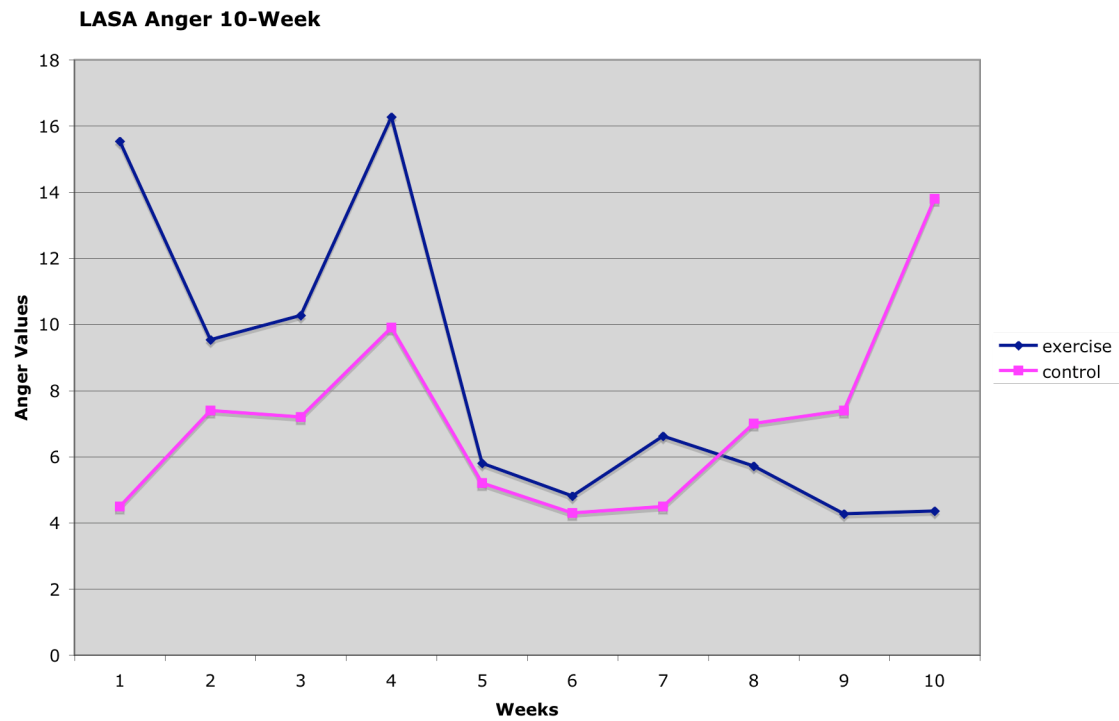
Appendix I

LASA Confusion Scale 10-Weeks



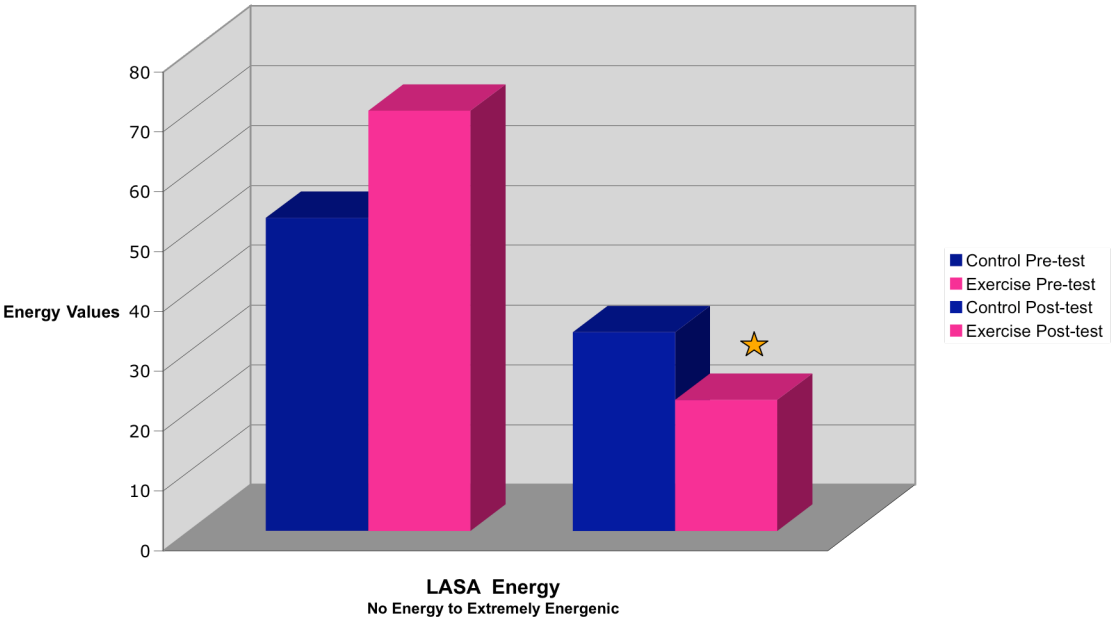
Appendix J

LASA Anger Scale 10-Weeks



Appendix K

LASA Energy Graph Pre-test/Post-test



Appendix L : Abstract Era of Hope 2005

The Effects of Low to Moderate Exercise Intensity Exercise on Fatigue in Breast Cancer Patients Following Clinical Treatment

K. Kemble, T. Burnham, B. Galucci

Fatigue is the most common symptom reported from cancer and cancer treatment. More than 70% of patients receiving chemotherapy or radiation reported fatigue symptoms including: tired legs, whole body tiredness, and feelings of wanting to lie down. Fatigue increases with the number of radiation or chemotherapy cycles. Several studies have investigated the effect of exercise on fatigue in cancer patients. Recent data suggests exercise can reduce fatigue in people surviving cancer. Little data however exists as to the appropriate intensity of exercise to reduce fatigue. Lower levels of exercise intensity may be as effective and better tolerated by patients who are suffering from extreme fatigue. The purpose of this study was to test the effect of low to moderate intensity exercise on fatigue and physical functioning in women who have completed treatment for breast cancer.

Nineteen women, ages 43-79, who had completed treatment for breast cancer, were randomly assigned to an exercise (n= 9) or control group (n = 10). The exercise group participated in a low-moderate intensity (30-50% heart rate reserve) aerobic exercise program 3 times a week for ten weeks. The control group did not participate in the exercise program. Physical functioning was measured by assessing peak aerobic capacity with a treadmill protocol. Both groups recorded their weekly level of fatigue using a Linear Analogue Self-Assessment Scale (LASA) and the Schwartz Cancer Fatigue Scale (SCFS).

Peak aerobic capacity increased significantly (32%, $p = .001$) in the exercise group. The control group showed a decrease of 5.7%. Fatigue reported with the Schwartz scale decreased in the exercise group and increased in the control group. This change was statistically significant between the groups ($p = .001$) and neared significance within the groups ($p = .06$). Fatigue reported with the LASA scale decreased in the exercise group and increased in the control group but the differences were not statistically significant between ($p = .21$) or within ($p = .36$) the groups.

This aerobic exercise program was effective in improving peak aerobic capacity and reducing fatigue (SCFS) in this group of breast cancer survivors. Fatigue measured by the LASA scale did not reach statistical significance partially due to the large variability around the means. These results are in the preliminary reporting stage of this project. This measure may reach significance as more subjects are entered into the study. Guidelines for an exercise intervention are already in place for chronic diseases such as diabetes and cardiovascular disease but no guidelines are in place for cancer patients and survivors. Lower intensity aerobic exercise should be considered for this population. Low to moderate intensity exercise is a safe, beneficial, efficient, and cost-effective tool for improving fatigue in breast cancer survivors.

The U.S. Army Medical Research and Materiel Command under DAMD17-03-0645 supported this work.

Appendix M: Abstract ACSM Annual Meeting 2006

Aerobic Exercise Decreases Depression and Anxiety in Breast Cancer Survivors

K. Kemble, T. Burnham

Breast cancer has a profound impact on women's health. There are many psychosocial effects including depression, anxiety, anger, and confusion. Depression and anxiety are common symptoms of survivors living with cancer and can adversely affect wellbeing and rehabilitation. **PURPOSE:** The purpose of this study was to test the effect of low to moderate intensity aerobic exercise on depression and anxiety in women who have completed treatment for breast cancer. **METHODS:** Twenty-two survivors of breast cancer (43-79 years of age, at least one month post-treatment) were randomly assigned to either an exercise group (n=12) or a control group (n= 10). The exercise group participated in a low to moderate intensity (30-50% heart rate reserve) aerobic exercise program three times a week for ten weeks. The control group did not participate in the exercise program. The Linear Analogue Self-Assessment (LASA) Scale was administered to subjects prior to the onset and at the conclusion of the ten weeks of exercise. This scale provides a measure of emotional distress and specifically includes measures of anxiety, confusion, depression, energy, and anger. **RESULTS:** Statistical analysis revealed a significant improvement depression ($p = .005$), anxiety ($p = .03$), confusion ($p = .04$), and anger ($p = .02$) in the exercise group compared to the control group ($p = .001$). There was no statistical difference between the groups on the measure of energy ($p = .19$). More specifically, depression decreased in the exercise group (23.0 ± 5.4 to 2.5 ± 1.1) and increased in the control group (7.6 ± 2.5 to 13.2 ± 6.1), anxiety decreased in the exercise group (31.5 ± 7.5 to 4.25 ± 1.6) and stayed the same in the control group (15.9 ± 6.8), confusion decreased in the exercise group (21.0 ± 5.1 to 6.3 ± 4.0) and increased in the control group (6.7 ± 2.0 to 10.7 ± 6.2), anger decreased in the exercise group (14.3 ± 6.2 to 4.0 ± 2.5) and increased in the control group (4.6 ± 1.4 to 13.8 ± 7.3). **CONCLUSION:** This aerobic exercise program was effective in reducing depression, anxiety, confusion, and anger in this group of breast cancer survivors. Guidelines for an exercise intervention are already in place for chronic diseases such as diabetes and cardiovascular disease but no guidelines are in place for cancer survivors. Low to moderate intensity exercise is a safe, beneficial, efficient, and cost-effective tool for improving depression and anxiety in breast cancer survivors.

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Appendix N

A. Kemble Thesis, University of Washington, Submitted June 2006.

Information in this thesis is presently being condensed into two manuscripts for publication. When completed, the manuscripts will be submitted as an addendum to this final report.

**Low to Moderate Intensity Aerobic Exercise Improves
Fatigue, Depression, Anxiety, and Aerobic Capacity in
Breast Cancer Survivors**

Katherine Kemble

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requirements for the degree of

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Abstract

Low to Moderate Intensity Aerobic Exercise Improves
Fatigue, Depression, Anxiety, and Aerobic Capacity in
Breast Cancer Survivors

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Chair of the Supervisory Committee:
Professor Betty Gallucci
School of Nursing

Purpose: This investigation examined the effects of a low to moderate exercise intervention on fatigue and overall QOL, both physiologically and psychologically in women who completed their breast cancer treatment. **Methods:** Twenty-two women, ages 43-79, who had completed treatment for breast cancer, were randomly assigned to an exercise (n= 12) or control group (n = 10). The exercise group participated in a low-moderate intensity (30-50% heart rate reserve) aerobic exercise program 3 times a week for ten weeks. The control group did not participate in the exercise program. Physical functioning was measured by assessing peak aerobic capacity with a treadmill protocol. Both groups recorded their weekly level of fatigue using the Schwartz Cancer Fatigue Scale (SCFS). The Linear Analogue Self-Assessment (LASA) Scale was administered to subjects prior to the onset and at the conclusion of the ten weeks of exercise.

This scale provides a measure of emotional distress and specifically includes measures of fatigue, anxiety, confusion, depression, energy, and anger.

Results: A repeated measures ANOVA showed peak aerobic capacity increased in the exercise group 32%, which was significant, between ($p = .0012$) and within ($p = .005$) in the groups. The control group showed a decrease of 4.8%. Body fat decreased significantly within the exercise group over time ($p = .0001$). Sit and reach increased significantly within the exercise group 10% over time ($p = .004$). Body mass index decreased in the exercise group and this difference neared significance within the exercise group over time ($p = .06$). Fatigue reported with the SCFS decreased 55% in the exercise group and increased in the control group. This change was statistically significant between the groups ($p = .0003$) and within the groups ($p = .01$). The decrease in depression in the exercise group (89%) neared significance ($p = .052$) and the difference between the two groups was significant ($p = .04$). Anxiety decreased significantly in the exercise group 86% ($p = .03$) and significantly different between the groups ($p = .01$). Confusion decreased significantly ($p = .04$) and anger decreased significantly ($p = .02$) between the exercise group compared to the control group. Energy increased 69% within the exercise group significantly ($p = .0005$). **Conclusion:** This aerobic exercise program was effective in improving aerobic capacity, lower-body flexibility, fatigue, depression, anxiety, confusion, anger, and energy in the exercise group of breast cancer survivors. Survivorship issues are quickly becoming a public health concern as more individuals are surviving cancer through advances in technology. Guidelines for an exercise intervention are

already in place for many chronic diseases but no guidelines are in place for breast cancer survivors. Low to moderate intensity exercise produced positive health benefits both physiologically and psychologically and should be considered as a safe, well-tolerated, rehabilitative tool for breast cancer survivors.

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DEDICATION

To my family, especially my husband, daughter, and dad for all their love and support, and to the memory of my mother.

Introduction

Specific Aims

A growing body of evidence suggests that cancer survivors who participate in an exercise program have substantially reduced cancer treatment-related symptoms. Cancer treatment-related fatigue is the most common complaint from cancer patients and has devastating effects. There are few published studies looking at the effects of physical activity on the reduction of fatigue for breast cancer survivors. We hypothesized that low to moderate (30-50% heart reserve) intensity aerobic exercise will improve fatigue, depression, anxiety, and increase aerobic capacity.

The specific aims of this study were to test the effect of low to moderate intensity aerobic exercise treatment on self-reported fatigue, depression, anxiety, and physical functioning in women who have completed therapy for breast cancer.

We hypothesized that women recovering from cancer therapy in the low to moderate exercise group:

1. Would increase aerobic capacity between the pre-treatment assessment and the assessment after 10 weeks and
2. Would decrease their self-reported fatigue, anxiety, and depression levels over the first 10 weeks of treatment compared to the control group.

Chapter I

Literature Review

Breast cancer has a profound impact on women's health. An estimated 211,240 women with invasive breast cancers were diagnosed in 2005. An additional 58,490 with breast cancer in situ were also diagnosed (American Cancer Society, 2006). The incidence of developing breast cancer is about 13% (1 in 8) by age 95 in the United States (DeVita, 2001).

Almost 9 million Americans are cancer survivors (Neiman, 2006). Cancer survival has increased steadily over the last 35 years for all cancers combined. An estimated 64% of those diagnosed with cancer can expect to be alive in 5-years compared to 1971 when long-term survival was estimated less than 50% (Demark-Wahnefried, 2005). As the numbers of survivors are increasing, so are the long-term health issues specific to cancer survivorship. This is rapidly leading to an emerging public health concern (Demark-Wahnefried).

Surviving breast cancer usually indicates that an individual has endured significant medical treatment. For this paper, women with the diagnosis of breast cancer who have completed their initial therapy will be defined as a cancer survivor. There are a growing number of people who are surviving the diagnosis of cancer as technology improves and early detection methods are implemented. The most recent estimate for 5-year survival is now 62% across all cancers and all disease stages (Courneya, 2003). Common cancers, if detected early, such

as breast, colon, and prostate now have a 90% survival rate (Courneya, 2003).

Survivorship issues are becoming increasingly important, including: improving quality of life (QOL), decreasing the risk of cancer recurrence, and promoting longevity in this population.

There are three primary treatments for breast cancer, which are surgery, radiation therapy, and chemotherapy (i.e. systemic drug therapy). These three treatments can be used independently or as combination therapy. There are many physiological and psychological side effects from cancer treatment. Side effects include fatigue, reduced cardiovascular and pulmonary function, muscle weakness and atrophy, weight change, difficulty sleeping, low blood counts, nausea, vomiting, and pain (Courneya, 2001). The side effects of cancer treatment are most intense during treatment, but will sometimes persist for months and even years (Courneya, 2001). Many of these negative side effects may be improved with exercise. Recent studies looking at the effects of exercise on physiological and psychological side effects from cancer treatment have concluded that exercise can be a useful rehabilitative tool (Burnham, 2002). Exercise can improve aerobic capacity, muscular strength, body composition, quality of life, decrease nausea, and fatigue (Courneya, 2002).

The American College of Sports Medicine (ACSM) recently published their 7th edition of guidelines for exercise testing and prescription and yet there are still no established guidelines for people wanting to exercise after cancer treatment (ACSM, 2006). Guidelines for an exercise intervention are in place, however, for

other chronic diseases such as diabetes and cardiovascular disease. Sedentary cancer survivors may be at increased risk for developing other diseases such as diabetes and heart disease. Recent data also suggests that sedentary cancer survivors may be at increased risk for cancer recurrence compared to active cancer survivors (McTiernan, 2004).

Specific exercise prescription guidelines for cancer survivors have posed many challenges for the ACSM, as there are so many different types of cancer and different therapies for each type. The lack of information on the underlying mechanisms of the benefits of exercise precludes the prescription of a precise mode, frequency, intensity, and duration of exercise (Nieman, 2006). Little data exists on the optimal length of time and most efficacious exercise intervention for cancer survivors. The ACSM has indicated that in healthy populations, important health benefits are realized in 15-20 weeks of regular exercise with marked improvements starting at 6 weeks (Kenney, 2000).

Research in this field is still minimal, but there is sufficient literature to now divide studies into two groups, during cancer treatment and after cancer treatment. It is important to differentiate these phases because of the likely differences in exercise prescription, safety, feasibility, and efficacy of the exercise intervention during these time periods (Courneya, 2003). There is also sufficient literature to divide studies into breast cancer survivors and non-breast cancer survivors. For this review, I focused on exercise studies with breast cancer

survivors and/or a mixed group of survivors (breast, colon, etc.) who have completed cancer treatment.

Physiological Aspects

Physical function is defined as the ability to perform routine activities of daily living. The Karnofsky Performance Status or Eastern Cooperative Oncology Group (ECOG) performance status criteria are used clinically to determine physical function in the oncology setting. These criteria are very general and are not sensitive to change over time (Schwartz, 2004). Moreover, they measure large changes in function such as performing routine hygiene and self care better than the ability of patient's to perform usual tasks (Schwartz, 2004).

MacVicar and Winningham (1986) were among the first to look at the effects of exercise on functional capacity during cancer treatment in a randomized controlled trial (RCT). They tested ten women with breast cancer on adjuvant chemotherapy who were randomized into two groups: an exercise group (n = 6), control group (n = 4). The supervised exercise intervention included 3 sessions per week for 10 weeks. The subjects performed cycle ergometry for 20 – 30 minutes at 60 – 85% of their maximum heart rate (MHR, defined as $220 - \text{age}$). Their exercise intervention became known as the Winningham Aerobic Interval Training (WAIT), which has been used in their subsequent research. Aerobic capacity was measured with a graded exercise test on the cycle ergometer. They also measured mood disturbance with the

Profile of Mood States (POMS), which is a 65-question rating scale evaluating fatigue, depression, anxiety, vigor, and confusion. Exercise capacity, as well as mood, improved from baseline in the exercising group but not in the control group from pre to post test analysis. For the purposes of this paper, I focused on exercise interventions after breast cancer treatment as opposed to interventions during treatment.

There are few interventional studies that look at the effects of physical exercise after breast cancer treatment (surgery, chemotherapy, and radiation). A randomized clinical trial by Courneya (2003) used a moderate to high intensity (70-75% VO_2 max) exercise intervention. The women ($N = 52$) were assigned to either a supervised aerobic exercise group or control group. The exercise group did cycle ergometer training 3-times a week for 15 weeks. They measured physical fitness (VO_2 max), quality of life (QOL) and fatigue using the Functional Assessment of Cancer Therapy-Breast Cancer (FACT-B) questionnaire, fasting insulin, body composition, insulin resistance, and insulin-like growth factors (IGFs). Their results showed peak oxygen uptake (VO_2) increased significantly ($p < .001$) in the exercise group and decreased in the control group. Overall QOL, happiness, fatigue, and self-esteem improved in the exercise group. The authors concluded that there were beneficial effects on cardiopulmonary function and QOL, but there was no significant effect on fasting insulin, IGF-1, and IGFBP-3.

Nieman et al (1995) studied the effects of an exercise program on breast cancer survivors who had undergone surgery, chemotherapy, and radiation. The

cancer survivors averaged 3 years post diagnosis. The subjects ($n = 12$) were randomly assigned to either an exercise group or a control group. The exercise intervention was a supervised training program that included 30 minutes of walking at 75% of MHR, and 7 different resistant weight-training activities with 12 repetitions each. A symptoms-limited exercise testing on a treadmill and 6-minute walk test was used to assess aerobic capacity (Galveo, 2005). Immunological responses were assessed by measuring natural killer (NK) cell activity and concentrations of circulating immune cells (Galveo, 2005). The results showed a significant improvement ($p = .02$) in the 6-minute distance walked group compared to the control group. There was no change in NK cell activity in either group. The small size ($n = 6$ per group) limited the ability to detect any significant differences between the groups.

Dimeo et al (1997) studied the effects of aerobic exercise on cancer survivors who completed high dose chemotherapy and autologous peripheral stem cell transplant. The subjects ($N = 32$) had mostly breast cancer, but also included non-Hodgkin's lymphoma, sarcoma, non-small cell lung carcinoma, or seminoma. The 32 subjects were evenly assigned into an exercise group or control group based on who lived closest to the testing center. The exercise intervention was supervised with subjects reporting 5-days per week for 6-weeks. The subjects walked a series of intervals on the treadmill with each lasting 3 minutes initially and progressed to 30 minutes of continuous walking at $90 \pm 5\%$ of their MHR. The control group did not participate in an exercise program. The

exercise group improved their maximum walking speed significantly by 0.72 km/hr ($p = 0.04$) compared to controls. Four subjects (25%) in the control group complained of increased fatigue while performing normal activities of daily living compared to the exercise group, which experienced decreased fatigue.

Limitations to this study were the lack of randomization, which causes selection bias. Also, the interaction between exercise and fatigue is difficult to gauge, as fatigue was not assessed with a standardized tool.

Pinto et al (2003) did a RCT with 21 breast cancer survivors who had stage 0, I, or II breast cancer and had completed surgery, chemotherapy, and/or radiation therapy. The women did aerobic exercise for 30 minutes 3-days per week for 12 weeks. The exercise intensity used was 60-70% of their heart rate reserve. The authors measured blood pressure (baseline and peak), and body self-esteem with the body esteem scale. The results showed baseline blood pressure, both systolic and diastolic improved as well as peak systolic blood pressure ($p = .05$). Physical condition and the weight concern subscale of the body esteem scale improved in the exercise group ($p = .03$). The control group was offered the exercise intervention at the conclusion of the study.

Burnham and Wilcox (2002) looked at the effects of aerobic exercise on physiological and psychological function in breast and colon cancer survivors rehabilitating from cancer treatment. The second purpose of their clinical trial was to evaluate the differential effects of low and moderate intensity exercise. The subjects ($N = 21$) were matched by aerobic capacity and scores on the Quality of

Life questionnaire then randomly assigned to either a low intensity (N = 7, 25-35% HRR), moderate (N = 7, 40-50% HRR), exercise program, or control group (N = 7). The exercise groups performed lower-body aerobic exercise for 10 to 32 minutes, 3-times a week. There were no statistically significant differences between the exercise groups so they were combined into one for group for final analysis. The results revealed statistically significant increases in aerobic capacity ($p < 0.001$) and lower-body flexibility ($P = 0.027$). Body fat decreased significantly ($P < 0.001$) with a significant increase in QOL ($P < 0.001$) and measure of energy ($P = 0.038$) in the exercise group. The authors concluded that low and moderate intensity aerobic exercise programs are equally as effective in improving physiological and psychological function with the population of cancer survivors they studied.

Psychological Aspects

There is a growing body of research looking at the effects of exercise after breast cancer treatment. The most common outcomes studied are biologic looking at the immune system, physical fitness, and lymphedema (Courneya, 2003). However, less attention is directed at psychological variables such as fatigue, depression, anxiety, mood, social well-being, self-esteem, satisfaction with life, and overall QOL.

The Rehabilitation Exercise for Health after Breast Cancer (REHAB) trial (Courneya, 2003) was a RCT looking at the effects of a supervised aerobic

training on aerobic capacity, QOL, and biologic outcomes in postmenopausal women who had completed surgery, chemotherapy, and radiation for breast cancer. Approximately half of the women were estrogen and/or progesterone receptor sensitive and on hormonal blockade during the exercise intervention. The women were randomly assigned to either an exercise group (n = 25) or control group (n = 28). The exercise group, at moderate intensity, trained on cycle ergometers 3-times per week for 15 weeks. The control group did usual care and did not train. They used a pretest and posttest design with primary outcomes of peak oxygen consumption assessed by VO_{2MAX} and QOL assessed by the Functional Assessment of Cancer Therapy-Breast (FACT-B) scale. Ninety-eight percent completed their trial with a 98% adherence rate amongst the exercise group. They found statistically significant changes in peak oxygen consumption, peak power output, overall QOL, happiness, fatigue, and self-esteem. Interestingly, they also proposed that some of the changes in QOL were mediated by positive changes in aerobic capacity (Courneya, 2003).

Courneya et al (2003) study, The Group Psychotherapy and Home-Based Physical Exercise (GROUP-HOPE) trial looked at whether a home-based exercise program could improve QOL beyond group psychotherapy. This was a mixed group of cancer survivors that were either going through cancer treatment (44%) or had recently completed cancer treatment (56%) for breast, colon, ovarian, or stomach cancer. The subjects were randomly assigned to group psychotherapy alone (n = 48) or group psychotherapy plus exercise (n = 60). The

exercise group did moderate intensity exercise, for at least 20-30 minutes, 3-5 days per week for 10 weeks. The control group doing psychotherapy alone were provided usual care only. Using a pre-test post-test design, physical fitness was assessed by using a submaximal treadmill test, sit-and-reach test, and a skinfold test. They used the Functional Assessment of Cancer Therapy-General (FACT-G) scale to measure QOL. The adherence rate was 84% in the exercise group with 89% completing the study. They found statistically significant improvement in functional well-being, fatigue, and sum of skinfolds. They found near significant results for physical well-being, satisfaction with life, and flexibility. This trial may be the first to use an exercise intervention with another validated QOL intervention in cancer survivors. The results showed that exercise might be a useful adjunct to psychotherapy for improving QOL, especially physical and functional well-being (Courneya, 2003).

Segar et al (1998) looked at the effects of exercise on breast cancer survivors using an experimental crossover design. The breast cancer survivors were women who had undergone surgical breast cancer treatment and averaged 3.5 years out. The women (n = 24) were randomly placed into an unsupervised gym or home-based self-paced aerobic exercise program, aerobic exercise program plus behavior modification, or control group. The exercise intensity was set at 60% of their MHR which they performed 30 minutes per day, 4-times a week, for 10 weeks. Outcome variables were measured with the Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), and the

Rosenburg Self-Esteem Inventory (RSE). The exercise groups had significantly decreased depression ($p < .01$) and anxiety scores ($p < .02$) compared to the control group. There were no differences between the exercise group and the exercise plus behavior modification group. Subjects who had recommendations from their oncologists to exercise had significantly higher adherence rates ($p < .02$) versus those who didn't. The control group, after the crossover, showed decreased depression and anxiety, which implied a positive psychological response with exercise.

Porock (2002) looked at the effects of a short-term home-based exercise intervention in a mixed population of cancer survivors (breast, colon, pancreas, oral, and melanoma). The training program appears to incorporate both aerobic and resistance exercises but the exact description of the intensity, frequency, and mode were missing (Galvao, 2005). The outcomes measured were fatigue, anxiety, depression, symptoms of distress, and QOL. Their results were positive showing a decrease in depression and anxiety but no change in fatigue. The limitations of this particular study included a small sample ($N = 9$) and a short exercise duration (4 weeks), but it stills represents a trend in positive adaptations with exercise.

Sandel et al (2005) looked at the effect of dance and movement on quality of life and shoulder function in breast cancer survivors ($N = 35$) treated within the prior 5 years. They conducted a RCT using a wait list control-crossover design. The 12-week exercise intervention used the Lebed Method: Focus on Healing

Through Movement and Dance. Outcome measures were the Breast Cancer Quality of Life (FACT-B), shoulder range of motion (ROM), and Body Image Scale. QOL (FACT-B) significantly improved ($p = .008$). The overall effect of training was significant at 26 weeks (time effect, $p = .03$) and the order of training ($P = .015$) (Sandel, 2005). They authors concluded that a dance movement program addressed the physical and emotional needs of women following breast cancer treatment.

Fatigue

Fatigue is by far the most common symptom reported in patients undergoing cancer treatment. Fatigue has been defined as complete lack of energy and severe mental exhaustion (Burnham, 2002). Fatigue, compared to all other side effects of cancer treatment has the most negative effect on quality of life and general well-being. More than 70% of patients receiving chemotherapy or radiation reported fatigue symptoms including: tired legs, whole body tiredness, and feelings of wanting to lie down. Fatigue increases with the number of radiation or chemotherapy cycles. Fatigue is associated with many diseases including cardiovascular disease, diabetes, depression, and cancer. Fatigue can cause coping mechanisms to fail, which negatively impacts physical functioning and hinders role functioning at home and work.

Bower et al (2000) looked at the occurrence of fatigue in a large number of breast cancer survivors ($N = 1,957$) in one of the largest-scale examinations of

fatigue in breast cancer survivors to date. Breast cancer survivors completed a survey study the RAND 36-item Health Survey. One third of the breast cancer survivors reported severe fatigue. This was associated with significantly higher levels of depression, pain, and sleep disturbance (Bower, 2000). Their study suggests that interventions, which treat depression and pain, may be useful in combating fatigue in cancer survivors. How much depression leads to fatigue or how much fatigue contributes to depression is still unknown.

Burgland et al (1994)) conducted a RCT with cancer survivors, which combined supervised group physical training (1-day a week for 4-weeks) with instructional and coping skills (1-day a week) totaling 7 weeks. The subjects (N = 60, 80% breast) completed adjuvant chemotherapy and/or radiation therapy within the prior 2 months. The exercise group improved on perceived physical strength and physical training post-test and continued to improve through the 3,6, and 12 month follow-ups. The exercise group had a lower physical training baseline however. At 12 months the intervention arm had significant improvements in physical status, strength, and sleep than controls (Denmark-Wahnefried, 2005). Both groups had decreases in fatigue and health problems.

Most breast cancer survivors go through a period of reduced activity after diagnosis and treatment. Women are significantly less physically active during the first year after diagnosis and treatment, and only 50% return to prediagnosis levels at 3 years (Irwin, 2005). What is not known is the extent to which fatigue contributes to a sedentary lifestyle or vice-versa.

The roll of exercise as a rehabilitative tool is now being investigated but the studies are still few in number. Clearly, more randomized trials are needed to validate the few and very significant studies of exercise, as an intervention, to promote physiological and psychological functioning, and particularly the influence on fatigue.

Summary

Research looking at the role of exercise as a rehabilitative tool for cancer survivors has only recently begun in earnest since the mid to late nineties (Courneya, 2003). Early research conducted in the eighties and on into the nineties mainly studied the effects of exercise during cancer treatment. During this time period, exercise may be considered more of a symptom management technique rather than as a rehabilitative tool. Trial designs were either observational or interventional, with more emphasis placed on physiological versus psychological outcomes.

With survival rates at 62 - 64%, long-term health issues specific to cancer survivorship are emerging as a public health concern. Survivorship issues have necessitated a major research effort in this field. The positive outcomes demonstrated in these studies support the need for second-generation studies directed at breast cancer survivors, which examine the type of exercise intervention, intensity, frequency, and optimal duration. This study attempted to

help establish an exercise regimen that will assist breast cancer survivors in improving their overall QOL, both physiologically and psychologically.

Chapter II

Methods

Subjects

Twenty-two women, ages 43-79, with breast cancer were recruited from Central and North Central Washington. North Central Washington is a rural area. Women had to drive up to 140 miles at the time of testing to participate. This study was part of a larger RCT, Burnham's "Exercise and the Effects on Quality of Life in Cancer Patients." Burnham's study looked at the effects of a supervised exercise program on quality of life and physical functioning in mixed population of breast, colon, and lung cancer survivors rehabilitating from cancer treatment.

To be included in this study the women were: a) 20-80 years of age, b) had stage I to III breast cancer, c) concluded treatment one to twelve months prior to enrolling, and d) were cleared to participate by their primary care provider. Women were excluded if they were being treated for other chronic diseases which would contribute to their fatigue such as congestive heart failure and poorly controlled diabetes.

Recruitment was done through advertising in newspapers, radio interviews, posters, and word of mouth. Posters about the study were placed in local community centers, medical centers, clinics, and hospitals in both Central and North Central Washington State. Initial screening was conducted by phone interview. Each subject was informed both verbally and in writing as to the

purpose and admission criteria of this study. Subjects who met admission criteria signed and received a copy of the informed consent.

Design and Procedures

At the first session, subjects were randomly assigned to either an exercise intervention group or usual care (control group) and demographics and baseline measures were obtained. Those assigned to the exercise group participated in a supervised low to moderate intensity (30-50 % heart rate reserve) exercise program 3 x week for 10 weeks. Baseline physical functioning was determined by measuring peak aerobic capacity (ml/kg/min) utilizing a walking treadmill protocol prior to randomization. They performed a second treadmill test 10-weeks after the initial treatment session. Women in both groups recorded their level of fatigue weekly using a Linear Analogue Self-Assessment Scale (LASA) and the Schwartz Cancer Fatigue Scale (SCFS). Participants were contacted by phone after the initial enrollment and between weeks 4-6 to check-in regarding how the program was going, answer questions, and promote compliance. Self-reported psychological measures were collected during the exercise program at week 5 and again at week 10 during the second treadmill testing.

Protocol for Exercise Intervention

The exercise intervention was a program designed specifically for breast cancer patients called the Lebed Method. Lebed-Davis developed a program

using ROM exercises to help reduce lymphedema in breast cancer survivors (Sandel, 2005) with a focus on healing through movement and dance. The Lebed Method combines structured exercises with dance movements.

A total of eight women, 2 registered nurses, 2 exercise physiologists interns from Central Washington University, and 2 breast cancer survivors were certified in the Lebed Method. The 8 women trained together and implemented the same routines which were taught at each session. For this study, the exercise programs were held 3-days a week, for 10 weeks, in Yakima, Ellensburg, Wenatchee, and Brewster, Washington.

At the initial visit, heart rate reserve was calculated and each woman was given a Polar heart monitor and instructed in its use. All the women were taught how to calculate their own heart rate reserve, given their target range, and told to exercise within the provided range ensuring that each participant exercised at 30 -50% of their heart rate reserve.

The Karvonen method for calculating heart rate reserve (HRR) was used as follows:

$$\text{Maximum heart rate (MHR)} = 220 - \text{person's age}$$

$$\text{Heart Rate Reserve (HRR)} = \text{Maximum HR} - \text{resting HR}$$

$$40\% \text{ HRR} = (\text{HRR} \times .40) + \text{RHR}$$

Example: age 50, resting HR 75, at 40% HRR.

$$220 - 50 = 170 \text{ (MHR)}$$

$$170 - 75 = 95 \text{ (HRR)}$$

$$(95 \times .40) + 75 = 113 \text{ at } 40\% \text{ HRR}$$

The HRR was calculated to provide the target heart range during the exercise intervention.

During each exercise session, the women spent the first 10-15 minutes doing aerobic warm-up exercises and stretching, which included head and neck stretches, arm circles, shoulder rotations, side-to-side arm extensions, and full-body contractions and extensions. This particular part of the exercise intervention helped facilitate lymphatic drainage and aided with lymphedema. The following 25-30 minutes incorporated low to moderate aerobic dance exercise (30-50% heart rate reserve). The dance movements were simple and no previous experience was necessary. Women became familiar with the workout music and routines. Upper body and extremity movements were performed to music with at least 4-6 repetitions each side. Stretch bands were also used to aid with resistance training. Lower body and extremity movements included side-to-side hip swings, dance steps utilizing forward and backwards flexion, extension, abduction, and adduction. This was followed by an aerobic cool-down (3-5 minutes) and stretching (7-10 minutes) for a total of 50-60 minutes per session. The procedure was modified for two women who lived 140 miles away. The women initially participated in the supervised exercise programs until they became familiar with the routines. When the two women become competent to do the routines on their own, they maintained the exercise routines, on the same schedule as other attendees, throughout the study. In some instances they also

used treadmills, stationary bicycles, or elliptical machines for the aerobic part of the program. The women continued to monitor exercise intensity using a Polar heart rate monitor (Target model). They both kept close contact by phone and submitted their weekly fatigue scales at weeks 5 and 10.

Measures

Demographics

Demographics, Health History, Cancer, and Exercise characteristics were determined (see appendix A and B). Questions included their previous medical history, medications, and current symptoms. Cancer characteristics included a short history of the onset of cancer, assessment, and treatment. Exercise characteristics included current and past exercise programs, frequency of exercise, duration, and preferences.

Physical Function

Physical functioning was determined by measuring aerobic capacity during treadmill testing. Subjects established a comfortable walking pace of 1.5 to 4 mph. The grade of the treadmill was increased 1% each minute and continued until the subjects reported volitional exhaustion. Heart rate was monitored during treadmill testing using a Polar heart rate monitor (Target model). Oxygen consumption was measured using an open circuit indirect calorimetry technique. The metabolic cart was calibrated to known

concentrations of oxygen and carbon dioxide prior to each test. The subjects breathed into a 2-way valve system during the test, which is connected to the metabolic cart for analysis. The subjects inhaled room air while their exhaled gases go directly into the metabolic cart. This process permitted quantification of expiratory volumes, O₂ concentrations, and carbon dioxide concentrations and the calculation of aerobic capacity ($\text{mL.kg}^{-1}.\text{min}^{-1}$).

Lower-body flexibility was measured using a modified sit-and-reach test (Hoeger, 1992) as described by the American College of Sports Medicine (2006).

Anthropometric

Body mass index (BMI) was calculated by dividing body weight in kilograms by height in meters squared (kg.m^{-2}). The percent of body fat was calculated as the sum of 3 skinfold measurements in mm. Skinfold measurements were taken using Lange calipers following procedures by Jackson and Pollock (1978) and the American College of Sports Medicine (ACSM, 2006). The sites measured on women were their triceps, suprailiac, and thigh. The standard error of the estimate is reported at $\pm 3.6\%$.

Psychological Distress and Fatigue

A modified Linear Analogue Self-Assessment Scale (LASA) and the Schwartz Cancer Fatigue Scale (SCFS) measured self-reported fatigue levels.

The LASA was derived from the Profile of Moods States (POMS). It includes 6 scales: fatigue, depression, anxiety, confusion, anger, and energy.

The LASA used a 100 mm line, that is anchored by the terms “not at all fatigued” and “extremely fatigued;” for energy levels “not at all energetic” and “extremely energetic.” The score is determined by measuring the placement of the mark on the line. Scores range from 0 to 100. Test-retest reliability of the scale 12 weeks apart in 60 cancer patients was $r = .61$ (Sutherland, 1988). Validity was based on the correlation with the original POMS, with the correlation $r = .79$.

The SCFS is a 6-item Likert scale which asks participants to rate the terms: tired, difficulty thinking, overcome, worn out, and listless as 1 “not at all,” 2 “a little”, 3 “moderately”, 4 “quite a bit” and 5 “extremely.” The SCFS demonstrated strong internal consistency reliability exceeding Cronbach alpha $> .85$ (Schwartz, 2002).

Statistical Analysis

Demographic data was measured by descriptive statistics (means and standard deviation). Aerobic capacity data was analyzed using a paired t-test. A two-way repeated measures ANOVA was used to determine if the changes to the self-reported fatigue and emotional distress levels were statistically significant. All values were reported as means and standard deviations. An alpha level of <0.05 was considered statistically significant. All analyses were conducted on StatView SE+ Abacus Concepts Inc. software.

Human Subjects

The institutional review board of Central Washington University approved the procedures of the larger study. The parent grant was modified to include this sub-study. Human subjects approval was obtained from both Central Washington University and from the University of Washington institutional review boards for this study. University of Washington Human Subjects application numbers were 02-3293-D 01, -D 02, -D 03, -D 04, and -D 05.

Chapter III

Results

Subjects' Characteristics

The mean age of subjects in the control group was 55 ($\pm$ 8.4 SD) and the exercise groups' mean age was 62 ($\pm$ 9.6 SD). The majority of women were diagnosed with stage II breast cancer. The control group had two women with Stage I breast cancer and Stage III respectively. The exercise group had four women with Stage I and one with Stage III disease. The control group had seven women who were estrogen receptor positive and three negative. The exercise group had nine women estrogen receptor positive and three negative. See Table 1 for demographic data and past medical history.

As shown in Table 1, the subjects in both groups all had standard treatment for breast cancer. The control group had 10 women treated by lumpectomy, followed by chemotherapy with doxorubicin, cyclophosphamide (N = 2), and paclitaxel (N = 2). One participant was treated with cyclophosphamide, methotrexate, and fluorouracil and one was treated only with the aromatase inhibitor, anastrozole. Nine out of the 10 women received radiation therapy. The exercise group had 2 women treated with mastectomy. The other 10 women were treated with lumpectomy, followed by chemotherapy with doxorubicin, cyclophosphamide (5 participants), plus paclitaxel (5 participants). Ten of the exercise group had radiation therapy. The control group had 7 women on

hormonal blockade with either tamoxifen or an aromatase inhibitor while the exercise group had 9 women.

The control group had 6 sedentary women, 1 who exercised irregularly, and 3 who exercised regularly. The exercise group had 6 sedentary women, 3 who exercised irregularly, and 3 who exercised regularly. No significant differences found between the groups for age, stage of their disease, hormone receptor status, treatment, exercise habits, or past medical history.

No subjects withdrew from either the control or exercise group. All subjects completed the ten-week study session and follow up measures. Over the 10 weekly exercise sessions the attendance rate averaged 94%. The exercise group had no reported problems or injuries.

Physiological measures

A repeated measures ANOVA showed peak aerobic capacity increased the exercise group by 31.5% (16.5 ± 8.1 to 21.7 ± 9.4). The control group, in comparison, showed a decrease in aerobic capacity of 4.8% (16.6 ± 5.1 to 15.8 ± 3.8). This change was statistically significantly between the groups ($p = .0012$) and within the exercise group over time ($p = .005$). See Table 2.

Body mass index (BMI) decreased in the exercise group (26.5 ± 4.1 to 26.2 ± 4.2). This change was not statistically significant between the groups but neared significance within the exercise group over time ($p = .06$).

Body fat percentage decreased in the exercise group by 4.7% (29.8 ± 3.7 to 28.4 ± 3.8). The change was statistically significantly within the exercise group over time ($p = .0001$).

Flexibility as measured by the sit and reach increased in the exercise group by 10% (30.9 ± 7.2 to 34.0 ± 4.9). This change was statistically significantly within the exercise group over time ($p = .004$).

Psychological self-reported measures

Results for psychological measures are listed in Table 3 and the weekly measurements are found in the appendices. Fatigue reported with the Schwartz Cancer Fatigue Scale (SCFS) decreased by 55% in the exercise group (17.8 ± 5.9 to 8.01 ± 3). Fatigue increased in the control group (11.8 ± 4.9 to 15.5 ± 8.3). This change was statistically significant between the groups ($p = .0003$) and within the groups ($p = .01$). Fatigue reported with the LASA scale decreased in the exercise group and increased slightly in the control group but the differences were not statistically significant between ($p = .17$) or within ($p = .10$) the groups.

Depression reported with the LASA scale decreased the exercise group by 89% (23.0 ± 19.0 to 2.5 ± 4.0). Depression increased by 73% in the control group (7.6 ± 8.1 to 13.2 ± 19.5). This change was statistically significantly between the groups ($p = .005$) and neared significance across time within the groups ($p = .052$).

Anxiety reported with the LASA scale decreased in the exercise group by 86% (31.6 ± 26.2 to 4.3 ± 5.7). This change was statistically significantly between the groups ($p = .03$) and within the groups over time ($p = .01$).

Confusion reported with the LASA scale decreased in the exercise group by 70% (21.0 ± 17.9 to 6.3 ± 14.1). Confusion increased by 60% in the control group (6.7 ± 6.6 to 10.7 ± 19.8). This change was statistically significantly between the groups ($p = .04$).

Anger reported with the LASA scale decreased in the exercise group by 71% (14.3 ± 21.5 to 4.1 ± 8.8). Anger increased over 200% in the control group (4.5 ± 4.7 to 13.8 ± 23.4). This change was statistically significantly between the groups ($p = .02$).

Lack of energy reported by the LASA scale improved in the exercise group by 69%. (70.2 ± 19.3 to 21.9 ± 30.0). This change was significant over time ($p = .0005$).

Table 1. Subject Characteristics (mean $\pm$ SD)

<i>n</i> = 22	Control (<i>n</i> = 10)	Exercise (<i>n</i> = 12)
Stage I	2	4
Stage II	6	7
Stage III	2	1
ER+	7	9
ER-	3	3
Type of treatment*		
Surgery	10	10
Lumpectomy	0	2
Mastectomy		
Chemotherapy		
AC	2	5
AC+Taxol	5	5
CMF	1	0
AI only	1	0
Radiation	9	10
Taking TAM or AI	7	9
Exercise		
Sedentary	6	6
Irregular	1	3
Daily	3	3
PMH*		
Unremarkable	3	2
Hypothyroid	3	6
HTN	3	3
DM	1	1
Hyperlipidemia	3	3
Osteoarthritis	3	2
SLE	1	0
COPD	0	1
Asthma	0	0

* Numbers may be greater or less than *n* due to combination therapy and diseases.

Abbreviations: ER, estrogen receptor, AC, Adriamycin, Cytosan, CMF, Cytosan, Methotrexate, 5FU, TAM, Tamoxifen, AI, Aromatase Inhibitor, PMH, past medical history, HTN, hypertension, DM, diabetes mellitus, SLE, lupus, COPD, chronic obstructive pulmonary disease.

Table 2. Physiological Measures (mean $\pm$ SD)

Dependent Variables	Pre-treatment	Post-treatment	% Change Pre - Post Treatment	P Values	
				AB	RM
Aerobic capacity (mL.kg ⁻¹ .min ⁻¹)					
Control	16.6 ($\pm$ 5.1)	15.8 ($\pm$ 3.8)	4.8%		
Exercise	16.5 ($\pm$ 8.1)	21.7 ($\pm$ 9.4)	-31.5%	.0012t	.005*
BMI					
Control	30.1 ($\pm$ 5.8)	30.0 ($\pm$ 5.7)	.3%		
Exercise	26.5 ($\pm$ 4.1)	26.2 ($\pm$ 4.2)	1.1%	.19	.06
Body fat %					
Control	33.4 ($\pm$ 5.3)	31.8 ($\pm$ 5.1)	4.8%		
Exercise	29.8 ($\pm$ 3.7)	28.4 ($\pm$ 3.8)	4.7%	.61	.0001*
Sit and reach(mm)					
Control	28.5 ($\pm$ 9.7)	30.7 ($\pm$ 7.3)	-7.7%		
Exercise	30.9 ($\pm$ 7.2)	34.0 ($\pm$ 4.9)	-10 %	.60	.004*

* Significant within (RM) group difference over time, $P < 0.05$.

t Significant between (AB) group difference, $P < 0.05$.

% Change = pre-post value/pre-value x 100

Abbreviations: SD, standard deviation, ml, milliliters, kg, kilograms, %, percent, BMI, body mass index, cm, centimeters,

Table 3. Psychological Measures (mean $\pm$ SD)

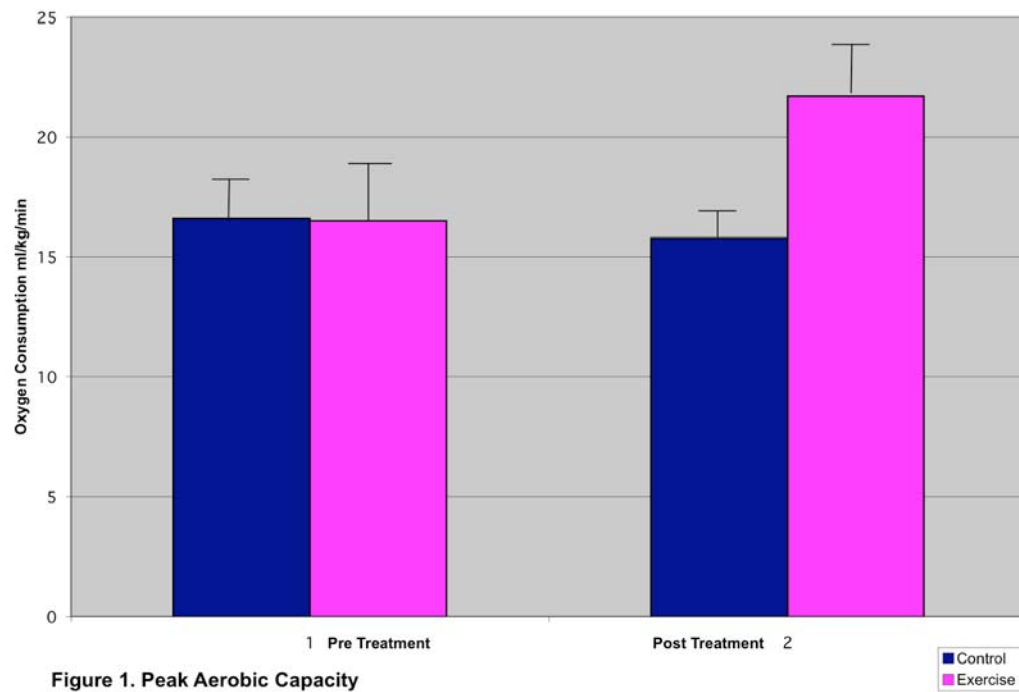
Dependent Variables	Pre-treatment	Post-treatment	% Change Pre to Post Treatment	P Values AB RM
SCFS Control Exercise	11.8 ($\pm$ 4.9) 17.8 ($\pm$ 5.9)	15.6 ($\pm$ 8.3) 8.1 ($\pm$ 3.4)	-32.2% 54.5%	.0003t .01 *
LASA Fatigue Control Exercise	31.30 ($\pm$ 15.9) 41.0 ($\pm$ 23.0)	31.33($\pm$ 34.6) 19.4 ($\pm$ 29.9)	-0.09% 52.7%	.10 .17
Depression Control Exercise	7.6 ($\pm$ 8.1) 23. ($\pm$ 19.0)	13.2 ($\pm$ 19.5) 2.5 ($\pm$ 4.0)	-73% 89%	.005 t .052
Anxiety Control Exercise	16.3 ($\pm$ 19.7) 31.6 ($\pm$ 26.2)	15.9 ($\pm$ 21.6) 4.3 ($\pm$ 5.7)	2.5% 86.4%	.03 t .01 *
Confusion Control Exercise	6.7 ($\pm$ 6.6) 21. ($\pm$ 17.9)	10.7 ($\pm$ 19.8) 6.3 ($\pm$ 14.1)	-59.7% 70%	.04 t .1
Anger Control Exercise	4.5 ($\pm$ 4.7) 14.3 ($\pm$ 21.5)	13.8 ($\pm$ 23.4) 4.1 ($\pm$ 8.8)	-206.7% 71.3%	.02 t .7
Lack of Energy Control Exercise	53.2 ($\pm$ 18.9) 70.2 ($\pm$ 19.3)	33.2 ($\pm$ 28.9) 21.9 ($\pm$ 30.0)	37.6% 68.8%	.17 .0005 *

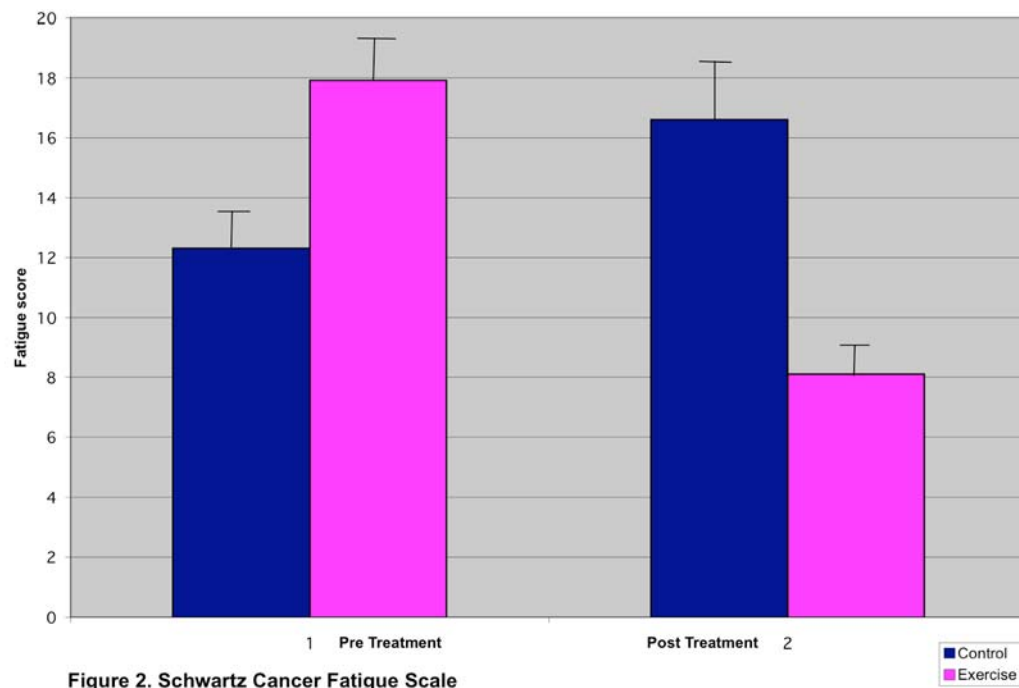
* Significant within (RM) group difference over time, $P < 0.05$.

t Significant between (AB) group difference, $P < 0.05$.

% Change = pre-post value/pre-value x 100

Abbreviations: SD, standard deviation, SCFS, Schwartz Cancer Fatigue Scale, LASA, Linear Analog Self-Assessment.





Chapter IV

Discussion

Many women are now surviving breast cancer thanks to advances in early detection and treatment options. As the proportion of long-term breast cancer survivors continue to grow, so do the long-term health issues associated with the cancer diagnosis and treatment. Survivorship issues are quickly becoming a public health concern. Cancer survivors are at a greater risk for developing secondary cancers and other diseases brought on by cancer treatment, genetic predisposition, and lifestyle factors. Cancer survivors are increasingly seeking information, counsel, and guidance to ensure a healthier life and perhaps longer one as well, (Denmark-Wahnefried, 2005). Epidemiologic studies have consistently demonstrated the benefits of low to moderate regular exercise to promote health and reduce morbidity (Schwartz, 2001). More research is needed for the development of guidelines, exercise prescriptions, and other rehabilitative tools for this rapidly growing population.

Cancer survivors often experience long periods of inactivity while going through cancer treatment. Inactivity leads to a progressive decline in aerobic capacity and results in decreased physical functioning. This greatly impacts the ability to perform activities of daily living. Health care providers frequently promote rest and recuperation to reduce side effects of cancer treatment. Fewer than 4% of them encourage cancer survivors to begin or continue an exercise program (Schwartz, 2004).

The purpose of this investigation was to examine the effects of a low to moderate exercise intervention on fatigue and overall QOL, both physiologically and psychologically in women who have completed breast cancer treatment. There is little research determining the optimum mode, frequency, intensity, and duration of exercise required for beneficial effects in this population. There is also little research comparing supervised exercise programs to home-based ones (Stevinson, 2004). Recent trends in exercise programs encourage modest levels of physical activity to achieve health benefits.

This study found that a low to moderate exercise program significantly improved physiological measures of peak aerobic capacity, body composition, and lower-body flexibility. These findings were similar to that of Burnham and Wilcox (2002) who found that exercising cancer survivors increased psychological functioning and improved overall quality of life, decreased fatigue and anxiety, and increased energy. Their low and moderate intensity aerobic exercise program over 10-weeks was effective in significantly improving aerobic capacity, decreasing body fat, and improving lower-body flexibility. Courneya (2003) has conducted several similar trials showing consistent significant improvements in aerobic capacity with measures of peak oxygen consumption. Dimeo (1997) and Pinto (2003) also had similar findings though their exercise programs that incorporated a moderate to high intensity aerobic exercise program. Most interventional studies have been 12-weeks or less. This study showed statistically significant benefits after a 10-week exercise program. It's

unknown whether the outcomes would have continued to show increased health benefits beyond 10-12 weeks duration.

This aerobic exercise program also significantly reduced psychological measures of fatigue (SCFS), depression, anxiety, confusion, and anger in this group of breast cancer survivors and increased their energy levels. These findings are consistent with other interventional studies with breast and mixed groups of cancer survivors. In the Rehabilitation Exercise for Health after Breast Cancer (REHAB) trial, Courneya et al. (2003), found significant decrease in fatigue, self-esteem, and over-all QOL. Courneya (2003) also found significant improvements in fatigue, improved functional well-being, and satisfaction with life in the Group Therapy and Home-Based Physical Exercise (GROUP-HOPE) trial. Segar et al (1998) had significantly decreased depression and anxiety in their exercise group compared to the control group. These studies, including, Porock (Galvao, 2005) and Sandel (2005), represent a consistent trend in positive adaptations with exercise.

Fatigue decreased significantly both between the groups and within the groups as measured with the Schwartz Cancer Fatigue Scale (SCFS). Fatigue measured by the LASA showed the same “trend” though it did not reach statistical significance partially due to the small sample. Increasing the numbers of subjects may also have increased the power of this analysis. The LASA scale may not be sensitive as the SCFS for measuring fatigue as it is a single item

where the SCFS is a six-item scale. Increasing the numbers of subjects may also have increased the power of this analysis.

Adherence

The exercise program utilized in this study was well tolerated by the participants. The adherence rates for attendance were also very high, averaging about 94%. This notably high adherence rate is consistent with other studies performed after completion of cancer treatment (Oldervoll, 2004). This may reflect a select group of cancer survivors who are interested in participating in a rehabilitative program after cancer treatment. Future studies should look at characteristics of the cancer survivors who decline to participate such as age, education, health habits, and level of fitness, body mass index, and mood.

Exercise programs for cancer survivors are often limited by the symptoms and residual side effects they experience from cancer treatment. The low to moderate intensity exercise intervention in this study did not exacerbate any symptoms we measured. The lower intensity levels may have allowed the participants to adapt more easily to exercise, which may be the reason the exercise sessions were well attended compared to other studies which used higher intensities. None of the participants withdrew or were injured which indicates that this population can exercise safely and effectively for extended periods of time.

The women who participated in this study were highly motivated. Greater than 50% who participated were sedentary women and did not exercise at all. The exercise intervention utilized in this study was a structured, supervised program, which guided them through a progressive exercise program specifically developed for breast cancer survivors (reduce lymphedema and increase range of motion). This may have also have promoted self-efficacy in addition to improved adherence in sedentary individuals.

A benefit that was noted was the development of a support system for the participants. None of the women were in support groups nor had any interest in joining such a group. The design of using a supervised exercise intervention became a major benefit as the women gained tremendous support from each other. This is consistent with other studies (Turner, 2004).

Strengths and Limitations

Limitations to this study include the small number of participants thus making it difficult to generalize the findings to larger and more varied populations of cancer survivors. More studies are needed with larger populations to evaluate the effectiveness of low to moderate exercise programs. The participants who volunteered may have been a healthier population thus making it difficult to generalize to other populations. Also, the sample was predominately Caucasian, further limiting generalizability as noted in similar studies (Schwartz, 2001). More subjects may have increased the statistical power of our analysis.

Strengths include that the sample was matched in regards to the stage of breast cancer and treatment. It was a randomized controlled trial. The control group was offered the exercise intervention when they completed the study so there was no demoralization, which may have affected the bias of the participants.

Summary

Prescription guidelines for an exercise intervention are already in place for chronic diseases such as diabetes and cardiovascular disease but no guidelines are in place for cancer survivors though aerobic exercise recommendations are now being suggested by the American Academy of Sports Medicine. Determining the optimal exercise prescription for the individual patient recovering from therapy is a large challenge awaiting future research (Neiman, 2006). Low to moderate intensity aerobic exercise should be considered for this population.

This study, consistent with several other studies, found that low to moderate intensity exercise produced positive health benefits both physiologically and psychologically. Exercise prescriptions, as in this study and others, should be utilized and encouraged for this population as a rehabilitative tool by health care providers.

The physiological improvements noted in this study may be responsible for the positive psychological effects women experienced. Improved aerobic capacity increased physical functioning, which is important in reducing fatigue

and improving quality of life in cancer survivors. This study demonstrated that a low to moderate exercise program helps reduce post-treatment related fatigue and emotional distress while improving physical functioning in breast cancer survivors.

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Appendix A

Medical History Questionnaire

Name:

1. Describe the type and stage of the cancer you are experiencing.

2. What type(s) of therapies were you receiving?

3. Are you experiencing any symptoms from your treatment? If so please list these symptoms (i.e. fatigue, nausea, brittle bones etc.)

4. Do you have any other health problems that may be aggravated by physical activity? If so please list these problems (i.e. cardiovascular disease, diabetes, respiratory problems etc.)

5. Are you currently on any medications? If so please list them.

Appendix B

Exercise History

- 1.** Are you currently participating in any sort of physical activity? If so, what type? If the answer to this question is no, please skip to question 4.

- 2.** How often (how many times per week) do you participate in an exercise program?

- 3.** In each individual exercise session how long do you exercise?

- 4.** Describe your exercise history to me. In other words, tell me about your past exercise experiences. This can be things like sports teams, walking programs, weight lifting, aerobics etc. If you have not exercised in a number of years, that's fine. Tell me what you liked to do for exercise as a teenager or even a child.

- 5.** What do you dislike about exercising?

Appendix C

Schwartz Cancer Fatigue Scale- 6-Item (SCFS-6)

The words and phrases below describe different feelings people associate with fatigue. Please read each item and circle the number that indicates how much fatigue has made you feel in the past **2 to 3 days**.

1 = not at all

2 = a little

3 = moderately

4 = quite a bit

5 = extremely

Tired	1	2	3	4	5
Difficulty thinking	1	2	3	4	5
Overcome.....	1	2	3	4	5
Listless	1	2	3	4	5
Worn out	1	2	3	4	5
Helpless	1	2	3	4	5

APPENDIX B**Linear Analogue Self-Assessment Scale (LASA)**

Developed by: Heather J. Sutherland, Patricia Walker, and James E. Till

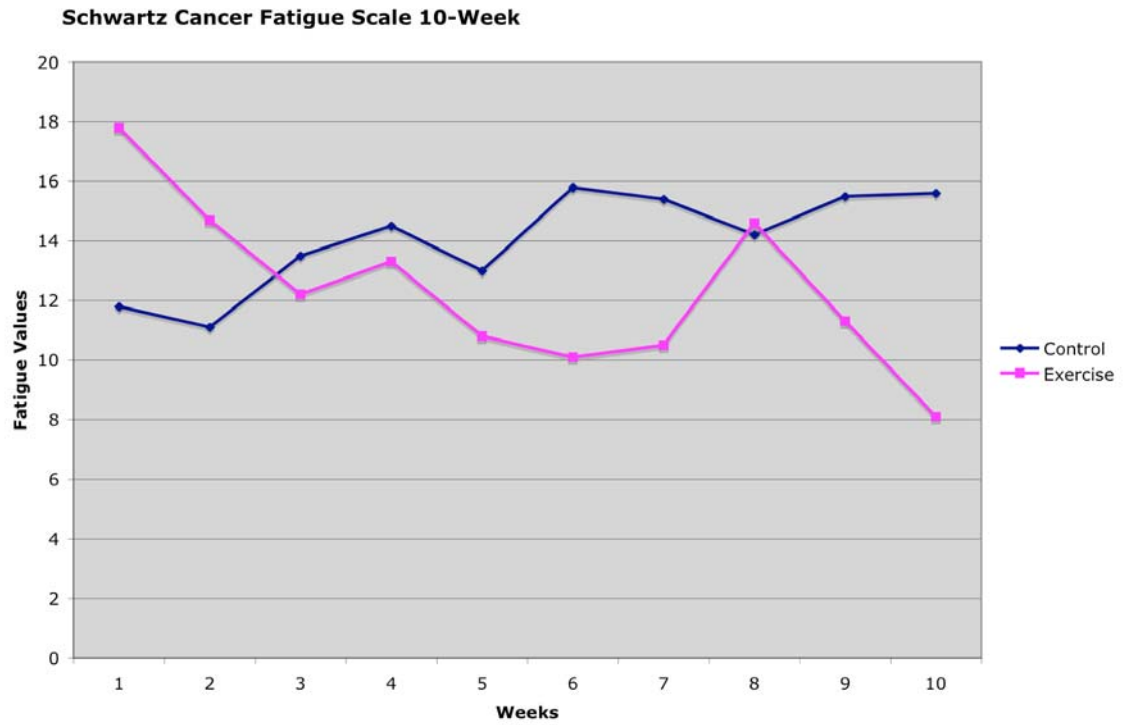
Instructions: Place a vertical mark on each scale at the position that best describes your state during the last week.

How have you been feeling during the past week?

- | | | |
|----------------------------|-------|------------------------|
| 1. Not at all
fatigued | _____ | Extremely
fatigued |
| 2. Not at all
anxious | _____ | Extremely
anxious |
| 3. Not at all
confused | _____ | Extremely
confused |
| 4. Not at all
depressed | _____ | Extremely
depressed |
| 5. Not at all
energetic | _____ | Extremely
energetic |
| 6. Not at all
angry | _____ | Extremely
angry |

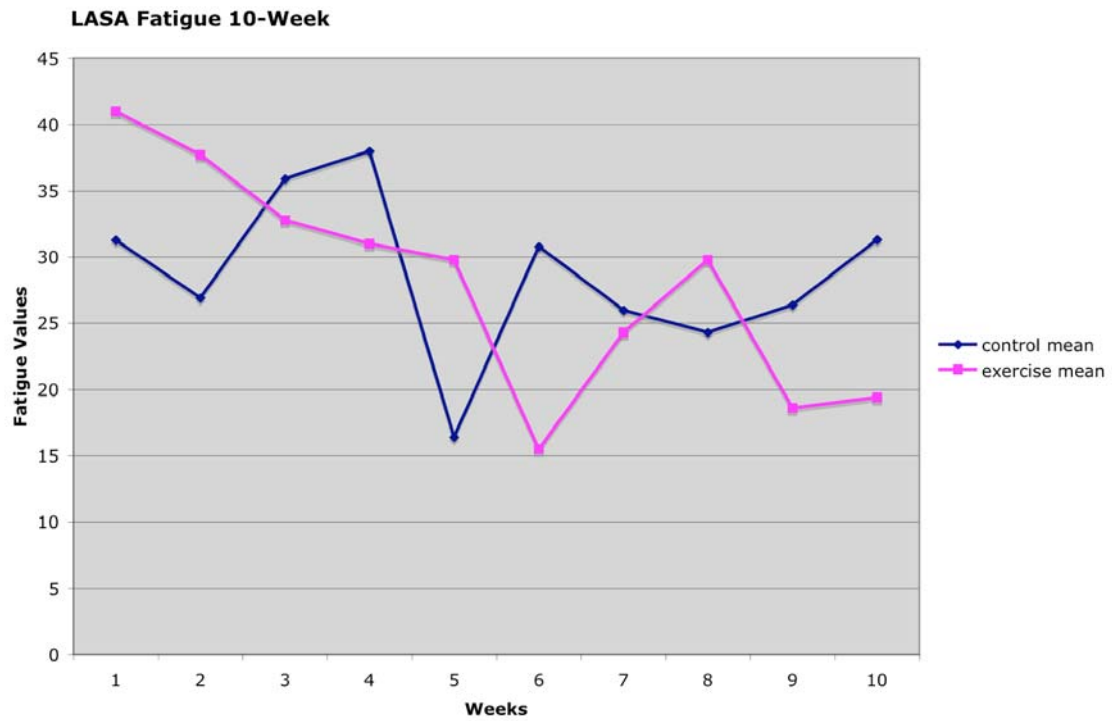
Appendix E

Schwartz Cancer Fatigue Scale 10-Weeks



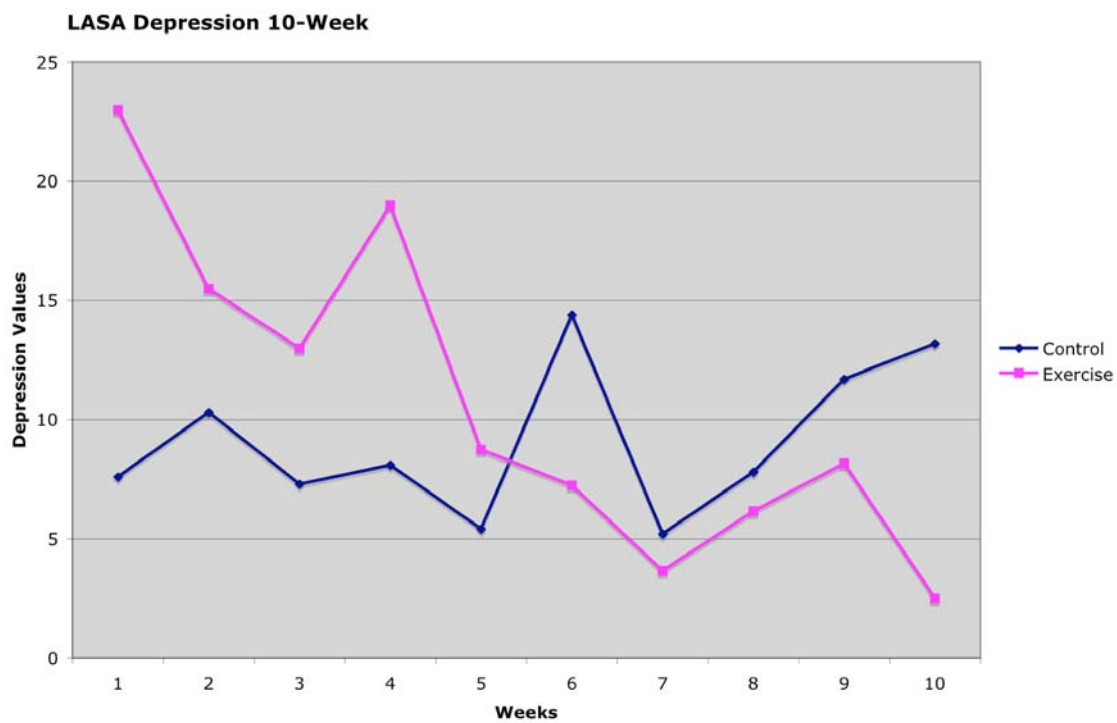
Appendix F

LASA Fatigue Scale 10-Weeks



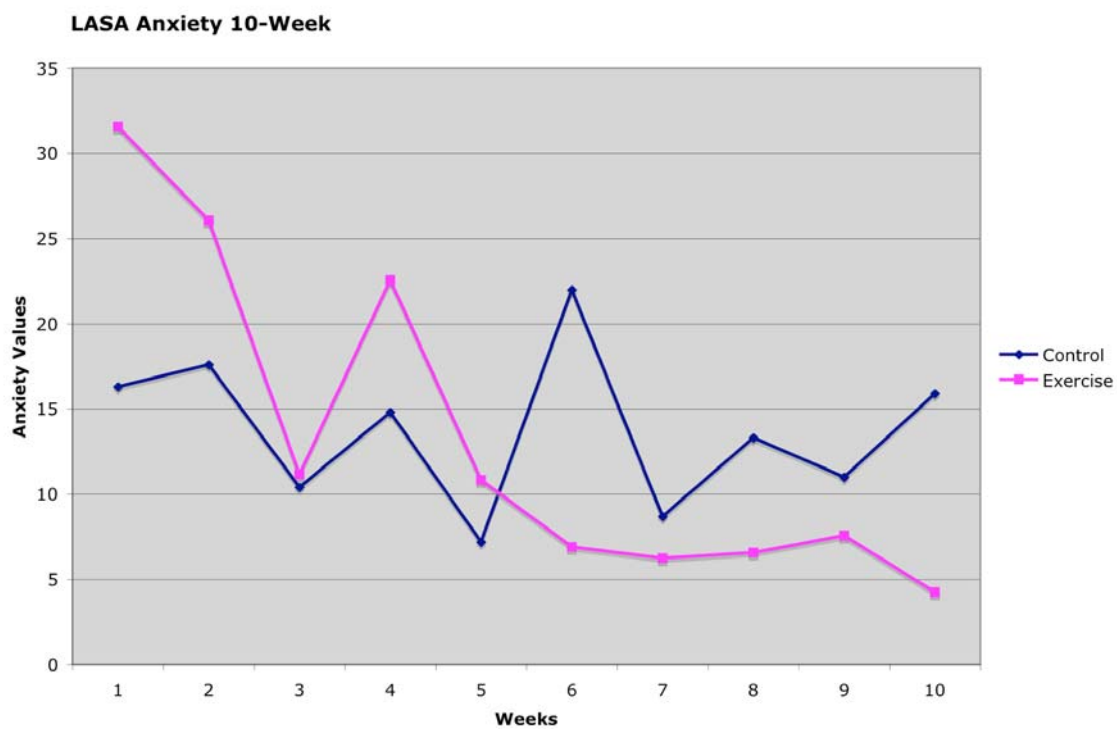
Appendix G

LASA Depression Scale 10-Weeks



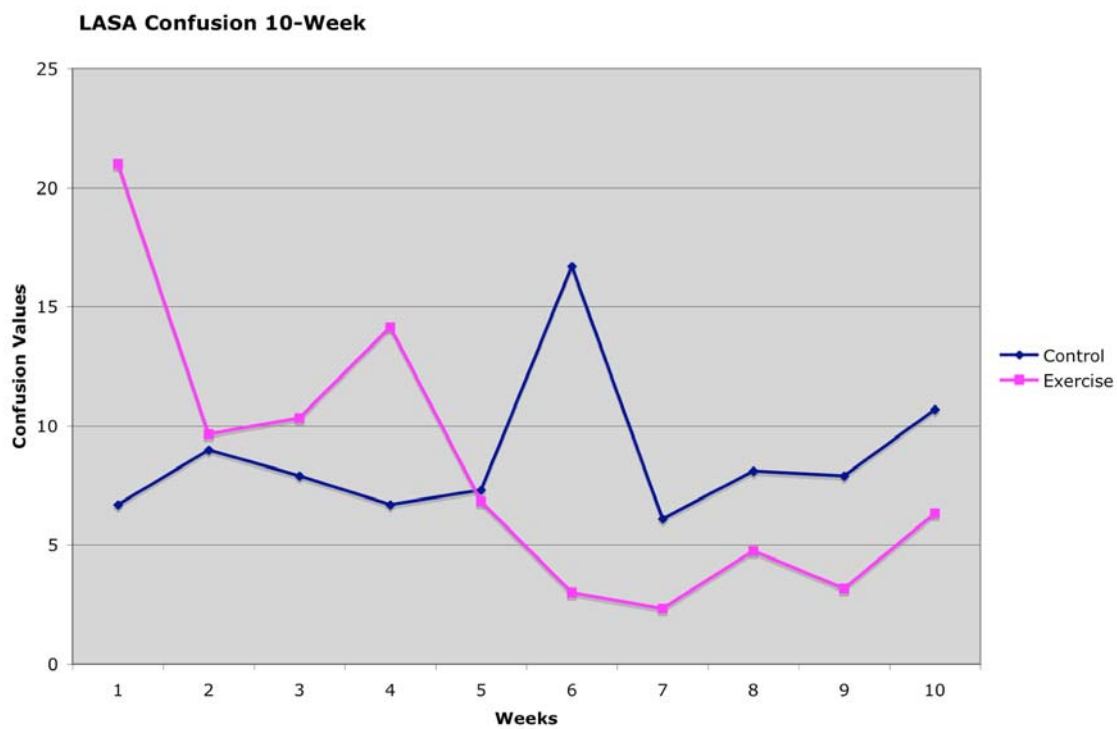
Appendix H

LASA Anxiety Scale 10-Weeks



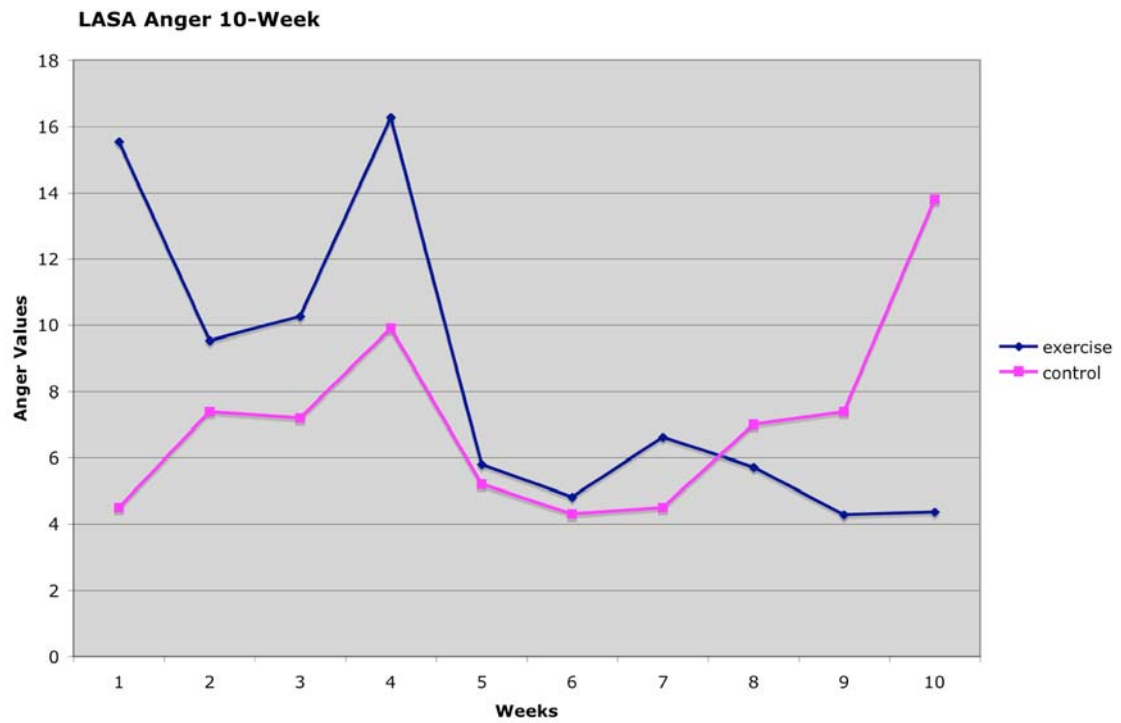
Appendix I

LASA Confusion Scale 10-Weeks



Appendix J

LASA Anger Scale 10-Weeks



Appendix K

LASA Energy Graph Pre-test/Post-test

