A PILOT STUDY OF RESISTANCE EXERCISE FREQUENCY IN BREAST AND OVARIAN CANCER SURVIVORS

by

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Submitted in partial fulfilment of the requirements
for the degree of Master of Science

at

Dalhousie University
Halifax, Nova Scotia
December 2014

Dedication

This thesis is dedicated to the memory of Andy Caldwell
and
to my grandmother Erma Gravelle.

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Abstract

A large body of research suggests exercise is effective for improving fitness, quality of life (QOL), and fatigue in cancer survivors. Despite evidence in support of exercise, few studies have rigorously evaluated exercise prescription for survivors. The purpose of this exploratory study was to critically evaluate the differences between a once-a-week and twice-a-week strength training program over a 13 week intervention. Eleven breast and ovarian cancer survivors were randomized to either once-a-week (n = 5) or twice-a-week (n = 6) strength training. Measures of upper and lower body strength and endurance, QOL, and fatigue were collected at the end of weeks 1, 7, and 13. No statistical differences in these primary outcome measures were found between the groups. However, independent of original group assignment, a significant group×time interaction was found for lower body strength (Wilks' Lambda=0.182, $F(2,8)$ 17.95, $p < 0.01$) and trends towards significance for upper body strength (Wilks' Lambda = 0.491, $F(2,8)$ 4.15, $p = 0.06$), fatigue (Wilks' Lambda = 0.501, $F(2,8)$ 3.99, $p = 0.06$), and physical functioning (Wilks' Lambda = 0.504, $F(2,8)$ 3.93, $p = 0.07$) when comparing survivors who attended at least once session/week with those who did not. No serious adverse events occurred. These results show that strength training is a safe and effective means for improving muscular strength and endurance. Because of the benefits to muscular fitness and QOL associated with training at least once a week, survivors should at least strength train once weekly and twice-a-week if possible.

List of Abbreviations Used

ACSM – American College of Sports Medicine

AE – Adverse Events

ANOVA – Analysis of Variance

CE – Cardiovascular Exercise

ES – Effect Size

FACT – Functional Assessment of Cancer Therapy

FIIT – Frequency Intensity Time and Type

GH - Growth Hormone

GLTEQ – Godin Leisure Time Exercise Questionnaire

HILV – High Intensity Low Volume

IGF – Insulin like Growth Factor

LBM – Lean Body Mass

LIHV – Low Intensity High Volume

MHC – Myosin Heavy Chain

MIMV – Moderate Intensity Moderate Volume

MOS-SF36 – Medical Outcomes Survey Short Form

mRNA – Messenger Ribonucleic Acid

MVPA – Moderate to Vigorous Physical Activity

MyoD - Myogenic differentiation 1 (a protein)

PDK4 - Pyruvate dehydrogenase lipoamide kinase isozyme 4 (an enzyme)

PSA – Prostate Specific Antigen

QOL – Quality of Life

RCT – Randomized Controlled Trial

RE – Resistance Exercise

ROM – Range of Motion

RPE – Ratings of Perceived Exertion

SLT – Standard Load Test

VO_2max – Maximum Oxygen consumption

1d/wk – Once-a-week training group

2d/wk – Twice-a-week group

1RM – One Repetition Maximum

6MWT – Six Minute Walk Test

%BF – Percent Body Fat

Acknowledgements

First and foremost I would like to thank the survivors who participated in this research study. It may seem odd to thank the survivors first, a position normally reserved for the thesis advisor or a loved one, but working on this project has taught me one thing; that research simply does not happen unless people volunteer as research participants. Thank-you for your time, patience and pushing through every painful set! What doesn't kill you makes you stronger, right? Next, I would like to thank my advisor Dr. Melanie Keats. Thanks for keeping me on track with so much going on all the time. Also, do you know how many times she's read through this damn thing? That's reason for thanks enough! I would like to thank my other committee members, Dr. Scott Grandy and Dr. Derek Kimmerly for always being around when I have questions. Dr. Blanchard and colleagues, thanks for the use of your lab! To the volunteers who helped with this study, your time and talents are appreciated and I wish you all the best in your careers as kinesiologists! To JC, thanks for the mentorship and helping me navigate life's obstacles, showing me what to do as much as what not to do (this is my public omission you did not flip off the police). To Dad and Grandma, thanks for bailing me out when I needed it! To the Dalplex, thanks for giving me a place to test the participants, a life change, a job, and for my Dalplex Family. To coffee, I need you, you complete me! To BT, you're the Andre to my Eric Wright, it's on for life!

Chapter One: Introduction

"According to the Canadian Cancer Society (2014), over 93,600 women will be diagnosed with cancer in 2014. While breast cancer will be the most common diagnosis for these women, representing 26% of new cases, gynecological cancers (ovarian, uterine, and cervical) represent an additional 10.9% of female specific cancer diagnoses. Fortunately, as more women are screened for these cancers through mammograms and Papanicolao tests, and as more effective cancer treatments are developed these cancers have become increasingly survivable. For example, 88% of women with breast cancer can now expect to survive five years or longer. It is for these reasons that cancer is more often considered a chronic disease that needs to be managed throughout the rest of a person's lifespan. Notwithstanding the impressive gains in survival, the side-effects of treatment, such as physical dysfunction (Hewitt, Rowland, & Yancik, 2003; Pinto, Trunzo, Reiss, & Shiu, 2002) and fatigue(Stone & Minton, 2008; Yellen, Cella, Webster, Blendowski, & Kaplan, 1997), are long lasting and highly prevalent in cancer survivors and can result in a lower QOL (Baker, Haffer, & Denniston, 2003; Graydon, 1994; Hanson Frost et al., 2000) and disability (Hewitt et al., 2003).

Fortunately, exercise is emerging as a promising recovery, coping, and management technique (Cramp, James, & Lambert, 2010; Galvao & Newton, 2005; Irwin & Ainsworth, 2004; Kim, Kang, & Park, 2009; McNeely et al., 2006; Oldervoll, Kaasa, Hjermstad, Lund, & Loge, 2004; Schmitz et al., 2005). However, as a relatively young field of research a number of gaps remain.

One limitation is that few studies have examined the benefits of resistance exercise (RE) or strength training in isolation (Irwin & Ainsworth, 2004; Schmitz,

Ahmed, Hannan, & Yee, 2005; Schmitz et al., 2005). Since RE shares a number of overlapping benefits with aerobics, such as improvements in fatigue and QOL(Cramp et al., 2010; McNeely et al., 2006), studies should isolate RE from the more commonly utilized aerobic exercises to more clearly identify what outcomes are improved by RE and the magnitude of such improvements. Thus far, RE has been shown in survivor populations to have several unique benefits beyond more traditional aerobic activities, including protection from bone loss and associated fractures (Winters-Stone et al., 2011) and improved symptoms of lymphedema (Kim, Sim, Jeong, & Kim, 2010; Lee et al., 2010). Additionally, it has been demonstrated that RE improves muscular fitness more than aerobics improve aerobic fitness (50-100% increase in one repetition maximums (1RM) vs. 6-8% improvements in VO_2max) (Courneya et al., 2007; Milne, Wallman, Gordon, & Courneya, 2008); yet both outcomes are important. Results of a meta-analysis, which excluded interventions with concomitant aerobic exercise, supports claims that resistance exercise increases muscle strength and size, body composition, and decreases in fatigue symptoms for cancer survivors (Strasser, Steindorf, Wiskemann, & Ulrich, 2013).

A second limitation is that much of the research that is available on exercise for cancer survivors focuses on breast cancer survivors (Irwin & Ainsworth, 2004). Perhaps this is because it is the most common cancer diagnosis among women and has a very high survival rate (88% are expected to survive five years or longer; Canadian Cancer Society, 2014). This presents a problem related to the generalizability of present research findings to other cancer types. To date, randomized controlled studies using resistance exercise interventions of other cancers specific to women, such as cervical, uterine, and ovarian,

are virtually absent from the exercise literature. This is perhaps because relative to other diagnoses, such as breast cancer, gynecologic cancers are less common and more challenging to study because there are fewer survivors. As a solution, previous studies that have used participants with gynecologic cancers include them with participants with other cancer diagnoses. Since the number of gynecologic cancer survivors in these studies is small, analysis comparing them to other cancer types is under powered making, it difficult to establish if these survivors have specific needs. A study of just breast and gynecologic survivors may be able to better establish if the benefits of RE seen in breast cancer survivors generalize to gynecologic cancer. Many of the benefits of exercise which are important for breast cancer survivors are likely also important for women with these diagnoses and there is little reason to suggest women with gynecologic cancers respond differently to exercise. These diagnoses have similar treatments, such as anti-estrogen therapies (e.g. aromatase inhibitors), and similar side-effects (e.g. body image concerns and sexual dysfunction). When one considers that only 17.5% of healthy women are strength training at least twice-a-week (Kruger, Carlson, & Kohl III, 2006), and participation in physical activity is lower in women who have had cancer (Blanchard, Courneya, Stein, & American Cancer Society's SCS-II, 2008) the need to include women who have had other cancer types in exercise research becomes apparent.

Finally, there are few controlled, experimental studies that have compared different exercise programs to establish which prescriptions are the most beneficial for improving the deleterious effects of cancer and its treatment (Buffart, Galvão, Brug, Chinapaw, & Newton, 2014). This is particularly problematic because current exercise guidelines have been based on guidelines for healthy individuals or people with other

chronic conditions such as heart disease (Schmitz et al., 2010). Furthermore, given that even the most recent meta-analysis only include 13 studies (Strasser et al., 2013), none of which directly compared interventions, there does not yet appear to be a body of evidence able to show what is optimal for cancer survivors. This has led to a number of inconsistent evidence based guidelines being published (Table 1) and creates considerable uncertainty for health care professionals, which may deter them from providing exercise recommendations (Jones, Courneya, Peddle, & Mackey, 2005). Related to this, most guidelines recommend an individualized approach to exercise prescription, but there is seemingly no information available to inform how to do this. Such information would come from studies that compare differing exercise programs and are able to identify interactions between participant characteristics (e.g. demographic, medical, baseline fitness, and quality of life) and group assignment (Buffart et al., 2014).

A recent position stand from the Australian Association for Exercise and Sport Science clearly states that these kinds of studies are needed to determine optimal, desirable, and necessary exercise and how to customize these guidelines to meet the needs of individuals (Hayes, Spence, Galvão, & Newton, 2009). Many studies have also echoed this need (Buffart et al., 2014; Donnelly et al., 2010; Fairey et al., 2005; Galvao & Newton, 2005; Irwin & Ainsworth, 2004; Jones, 2011; Lee et al., 2010; McNeely et al., 2006; Milne et al., 2008; Schmitz et al., 2010; Schwartz, Mori, Gao, Nail, & King, 2001; Schwartz, 2008; Speck, Courneya, Mâsse, Duval, & Schmitz, 2010; Stevinson, Lawlor, & Fox, 2004; Strasser et al., 2013; Winters-Stone et al., 2012). Despite such a large demand for studies of exercise prescription for cancer survivors, little has been done to address this need.

Table 1. Summary of various RE guidelines from available literature.

Source	Freq.	Intensity	Volume	Progression
Courneya et al., (2002)	3	Very light weight	2 sets of 10	Progress to 2 sets of 15 then 3 sets of 15 before adding weight; increases should be small
Courneya et al., (2004)	2+	NR	10-15 reps	Increase reps
Galvao & Newton (2005)	1-3	50-80% 1RM	1-4 sets of 6-12 reps	NR
Lucia et al., (2003)	2	Low	10-15 reps	NR
Schmitz et al., (2010)	2	Very low resistance	8-12 reps	Increase resistance in small increments; no upper limit on weight survivors' can lift
Schwartz (2008)	2-3	50%1RM	2-3 sets of 10-12 reps	Not Specified
Durst (2009)	2-3	40-60%1RM	1-3 sets of 3-5	Progress to 8-15 reps/set
Smith (1996)	NR	Low	High	Not specified

Note: Prescription variables refer to what is recommended when beginning the program. Freq = Training frequency in sessions per week. NR = Not Reported/Specified. 1RM = One repetition maximum.

A comprehensive search of the available literature returned only one other study which directly compared two RE programs (Cunningham et al., 1986) and one meta-analysis (Strasser et al., 2013). The first study (Cunningham et al., 1986) was with leukemia survivors on treatment and compared three sessions-a-week versus five sessions-a-week and a non-exercising control group. This study concluded that there were no significant differences in arm muscle mass between any of the groups after five weeks

of RE. Other outcomes important to survivors such as strength, QOL, and fatigue were not measured. The authors suggested that this was due to large within-group differences masking the significant effect of the prescriptions. Other limits in this study of leukemia survivors should be noted. First, a five week long intervention is not usually sufficient time to observe hypertrophy as early adaptation to RE is usually neural (Phillips, 2000). Irwin & Ainsworth (2004) recommend that exercise interventions for survivors last a minimum of 12 weeks to allow adaptation to occur. Additionally, the RE prescription used in this study (nine exercises done for one set of 15 repetitions at an unspecified resistance) may be limited by its low training volume. It has also been acknowledged that exercise may not be as effective during cancer treatment as it is afterwards (McTiernan, 2004).

The second study, a meta-analysis by Strasser and colleagues (2013), specifically attempted to determine the benefits of resistance exercise in isolation from aerobic modes and to determine a dose response. From this study, it was first established that resistance exercise was able to improve muscular fitness, body composition, and fatigue in adult cancer survivors. No dose response for any outcome was found for the effect of training volume. However, a positive dose-response was found for intensity and body fat percentage ($p = 0.02$) and a negative response for intensity and upper body strength ($p = 0.04$) with 60-70% of one repetition maximum (1RM) being considered optimal. This is surprising given that most studies of apparently healthy adults show strength gains are highest when heavier weights are used (Campos et al., 2002). As of this writing, three ongoing studies are currently examining the impact of resistance exercise intensity on

survivor outcomes (Buffart et al., 2014). The issue of training frequency was not addressed in Strasser's meta-analysis study.

Training frequency is potentially an important aspect of the training prescription for cancer survivors. Given that previous studies have reported that limited time reduces adherence in this population (Courneya et al., 2005; Rogers, Courneya, Shah, Dunnington, & Hopkins-Price, 2007), establishing a minimal training frequency is critical for minimizing time commitments for survivors and maximizing program adherence. Once-a-week RE has been recommended to be effective for chronically ill populations (Heyward & Gibson, 2014), yet, only one study (Lee et al., 2010) has used a once-a-week frequency in support of this claim's applicability to breast cancer survivors. More often, studies in this field employ training frequencies of 2-3 days per week. While it is likely that a survivor would be more able to adhere to one training session per week, if the training frequency is not high enough some level of detraining may occur between exercise bouts which would limit improvements in muscular fitness and QOL. Consequentially, a direct comparison of once-a-week and twice-a-week training frequency is warranted

An improved understanding of what constitutes an optimal exercise program will ultimately lead to a higher QOL for survivors. It is the opinion of this author that optimal exercise for cancer survivors should include the following features. First, improvements in important survivorship outcomes are maximised by the exercise prescription. Second, survivors are able to adhere to the exercise program. Third, individualization of the exercise prescription is possible and based on evidence-based research. Finally, adverse events (AE) and time commitment to exercise are minimised.

Given the dearth of evidence related to the generalizability of RE to gynecologic cancers, known upcoming studies examining training intensity, and the high value of studies comparing exercise prescriptions in cancer survivors that provide essential information about the benefits of RE. The purpose of the present study was to examine the effect of training frequency by comparing once-a-week RE against twice-a-week RE in a sample of female cancer survivors who have completed primary cancer treatment for either breast, cervical, uterine, or ovarian cancer. It was hypothesized that after 12 weeks both training groups would experience significant improvements in muscular fitness, physical functioning, body composition, QOL, and symptoms of fatigue. Because healthy, untrained individuals benefit more from twice-a-week than once-a-week RE (Peterson, Rhea, & Alvar, 2005), it was further hypothesized that the improvements in the twice-a-week group would be significantly greater than those experienced by the once-a-week group. It was hoped, that while preliminary, the results of this study will help inform RE guidelines for cancer survivors and encourage others to study exercise prescription in this population.

Chapter Two: Literature Review

Together, breast and gynecological cancers represent 36.1% of the 93,600 new cases of cancer in Canadian women (Canadian Cancer Society, 2014). The survival rates for these cancers continue to improve by approximately 2% per year due to advances in early detection through mammograms, Papanicolaou tests, and more effective treatment regimes. Breast cancer is the most commonly diagnosed of these cancers and it also has one of the highest survival rates at 88%; similar to ovarian cancer if detected early. While higher survival rates are encouraging, there is a growing population of survivors[1] and a whole new set of health concerns have become evident. These challenges include coping with the adverse effects of cancer treatment (e.g., decreases in muscular health and physical functioning, mental health, and QOL with increases in fatigue and adiposity) and promoting long-term health (e.g., reduce risk of cancer recurrence and co-morbid disease) (McTiernan, 2004).

While several treatment options are available, treatment of breast and gynecological cancers usually involves some combination of surgery, chemotherapy, radiotherapy, and hormone based treatments (Durst, 2009). Surgery for women with breast cancer may involve mastectomy, lumpectomy, lymph node dissection, and oophorectomy (removal of ovaries may also be done for breast cancer) and hysterectomy for women with gynecological cancers. These surgeries may cause pain, fatigue, early menopause and infertility, changes in body composition, mobility issues, lymphedema and psychological changes (Andrews & von Gruenigen, 2013; Grover et al., 2012).

[1] Note: the term 'survivor' in this thesis refers to anyone who has received a diagnosis of cancer and remains alive regardless of treatment status in accordance with terminology used by the National Coalition for Cancer Survivorship, 2012.

Chemotherapy involves the systemic use of toxic substances to kill cancer cells and side-effects may include: pain, fatigue, cardiotoxicity, changes in body composition, and may negatively affect bone health (Grover et al., 2012). Radiotherapy can be either done before or after surgery and could also be done during chemotherapy to target cancer cells. Radiotherapy has been known to cause fatigue, pain, mobility issues, and lymphoedema (Graydon, 1994). Lastly, hormone based treatments act by restricting hormones that tumours need to grow and side-effects mainly include fatigue and changes in body composition. These side-effects may persist for many years after treatment and also impair QOL (Baker et al., 2003; Graydon, 1994; Hanson Frost et al., 2000), physical functioning (Hewitt et al., 2003; Pinto et al., 2002), and physical activity levels of survivors (Pinto et al., 2002).

Over the past two decades exercise has emerged as an effective and safe management technique that improves many of the adverse effects associated with a cancer diagnosis and treatment (Jones, 2011). Specifically, several reviews of exercise interventions with survivors both on and off treatment have found that exercise in general can improve a survivors' QOL, fatigue, mental health, body composition, and fitness (Beesley, Eakin, Janda, & Battistutta, 2008; Buffart et al., 2014; Courneya, Karvinen et al., 2005; Cramp et al., 2010; Fitzgerald, 2007; Galvao & Newton, 2005; Kim et al., 2009; McNeely et al., 2006; Oldervoll et al., 2004; Pekmezi & Demark-Wahnefried, 2011; Schmitz et al., 2005; Stevinson et al., 2007).

While the number of studies examining the benefits of exercise for cancer survivors has increased in recent years, few have critically examined the basic principles of exercise training (Buffart et al., 2014; Campbell, Neil, & Winters-Stone, 2012).

Moreover, the large majority have focused primarily on aerobic exercise and relatively few have explored the unique effects of RE training (Irwin & Ainsworth, 2004; Schmitz et al., 2005). Consequently, the benefits and risks of RE are not fully understood, nor are they well known amongst health care providers. This is problematic as these professionals may be less likely to recommend RE to survivors if they do not see RE as beneficial. The following review will summarize the evidence of the known benefits of RE, as well as address issues of safety and adherence. Moreover, while detailed evidence-based recommendations are lacking for cancer survivors, several generic exercise and RE guidelines have been published and are also reviewed below.

The intent of this review is to highlight the potential unique benefits and risks of RE and as a consequence only studies that have included at least one arm of isolated RE will be included. The rationale for this approach is based on the large body of evidence which supports the use and safety of aerobic exercise to improve QOL and reduce treatment related side-effects and any studies using a combined aerobic and RE focus are not able convey the unique and overlapping benefits and potential risks associated with RE. A description of interventions and an overview of the studies reviewed can be found in Tables 2 and 4. Additionally, readers should be aware that this review identified two distinct times when a survivor may begin RE; during and after cancer treatment. This is because survivors who have completed treatment may differ from those on treatment with respect to exercise tolerance, motivation, ability to adapt to exercise, severity of treatment side-effects, and psychological and physical stress (McTiernan, 2004).

Resistance Exercise During Treatment

To date, four studies have examined the impact of a RE intervention during cancer treatment (Courneya et al., 2007; Cunningham et al., 1986; Galvao et al., 2006; Segel et al., 2003) (Table 2). Given the relative dearth of data, no definitive conclusions can be made, however each of the four studies provide preliminary evidence to suggest there are benefits for those undergoing active treatment.

Muscular fitness.

Three of the four studies reviewed assessed muscular strength and endurance (herein referred to as muscular fitness) as a primary outcome (Courneya et al., 2007; Galvao et al., 2006; Segel et al., 2003). As each study utilized a different measure of muscular fitness a direct comparison is difficult, however all of the interventions demonstrated benefit. Specifically, Courneya and colleagues found significant improvements in chest press (mean increase of 8.8kg or 35%, $p < 0.01$) and leg extension 1RM (mean increase of 8.2kg or 25%; $p < 0.01$) compared to controls and an aerobic exercise group. Segal and colleagues (2003) found that men undergoing androgen deprivation therapy for prostate cancer were able to increase the number of chest press repetitions that could be done with a 20kg bar (mean increase of 13.1 reps or 42%; $p < 0.01$) and leg presses with a 40kg load (mean increase of 11.8 reps or 32%, $p < 0.01$). The usual care controls experienced a decrease in chest press and leg press performance (-2.6reps and -1.6 reps respectively). Subsequent analysis showed that the benefits of RE were not affected by intent of treatment (curative vs. palliative) or how long the participants were on treatment. The study conducted by Galvao's research team (2006) used both the 1RM and standard load methods and reported significant improvements in

Table 2. Summary of randomized experimental trials during cancer treatment.

Study	Participants	Design	Length	Freq.	Sets/Reps	Intensity	Results
Courneya et al., 2007	Breast I-IIIa (n=242)	3 Arm RCT RE CE No Exercise	17±4 Duration of Treatment	3	3/8-12	60-70%1RM	↑Bench press and leg extension 1RM, LBM, Completion of Therapy, SE – QOL, Fatigue, %BF, Anxiety, Depression
Cunningham et al., 1986	Acute Leukemia (n=30)	3 Arm RCT 3d/wk RE 5d/wk RE No Exercise	5	3 & 5	1/15	NR	– Body Weight, Arm Circumference, Nitrogen balance
Galvao et al., 2006	Prostate (n=10)	Pre-Post	20	2	2-4/6-12	70-85%1RM	↑Bench press and leg press 1RM, Chest press and leg press standard load test, Physical functioning, balance – LBM, body fat, PSA, testosterone, GH
Segal et al., 2003	Prostate I-IV (n=155)	RCT RE Waitlist	12	3	2/8-12	60-70%1RM	↑Chest and leg press standard load test, FACT P ↓Fatigue – Body composition, PSA

Note: Length refers to the length of intervention in weeks. Freq = frequency in days/week. RCT = randomized controlled trial. RE = resistance exercise. CE = cardiovascular exercise. 1RM = one repetition maximum. LBM = lean body mass. SE = Self-Esteem. QOL = quality of life. FACT P = functional assessment of cancer therapy, Prostate. GH = Growth Hormone. PSA = prostate-specific antigen.
↑increase
↓decrease
— No change

1RM chest press and leg press which improved by 12.1kg (40.5%) and 76.7kg (96.3%) respectively, and the number of repetitions that could be done for these two exercises with a load equal to 70% 1RM at baseline increased by 11.2 (114.9%) and 26.8 (167.1%).

Body composition.

While all four studies assessed some measure of change in body composition, direct comparison across the studies is again difficult as several different measures were used. These included, body weight, body mass index, waist circumference, skinfolds, and lean body mass (LBM) (both dual x-ray absorptiometry and calculations of arm muscle area from arm circumference and skinfolds). Of the four studies, only one noted an improvement in body composition (Courneya et al., 2007). Specifically, Courneya and colleagues found that their RE intervention resulted in a 1kg increase in LBM ($p < 0.01$). This differs from what was found in Cunningham's study (1986) which did not observe a significant increase in muscle mass of the arms. However, Cunningham did report a correlation between arm muscle area and calories received through parenteral nutrition, indicating that sufficient calories are needed during treatment to maintain muscle mass. It is worth noting that the intervention in this study may not have been sufficient to cause change as most RE guidelines that are available for survivors recommend at least two sets of each exercise be completed (Courneya, Mackey, & McKenzie, 2002; Durst, 2009; Schmitz et al., 2010; Schwartz, 2008); this standard was not met in Cunningham's study where only one set was prescribed. Additionally, Irwin and Ainsworth (2004) reviewed the methodology used in exercise studies of cancer survivors and recommended that exercise interventions for persons with cancer should last a minimum of 12 weeks in

order to allow the benefits of exercise to develop and become observable; Cunningham's intervention was only five weeks long.

Quality of life.

QOL is a multidimensional measure of individual's well-being, often capturing aspects of well-being related to physical, mental and emotional health (Table 3). Overall, QOL was examined in both the Courneya (2007) and Segal (2003) studies. Both used the Functional Assessment of Cancer Therapy (FACT) system to measure QOL. The FACT system is a widely used questionnaire for measuring QOL and includes sub-scales for assessing physical, social/family, emotional, and functional wellbeing as well as fatigue and cancer site specific concerns (Yellen et al., 1997). Only Segal's study of prostate cancer demonstrated a significant difference between groups ($p < 0.01$). In this study, those given the intervention improved their FACT-P (prostate specific QOL scale) scores by 2 points while the control group's scores decreased by 3.3 points. This difference remained significant regardless of treatment intent (curative or palliative) or how long the participants had been on treatment.

Regrettably, neither of the above studies described changes in QOL in reference to the subscales of the FACT questionnaire. This is a limitation as resistance training my exert its effects more in areas of QOL that relate more to physical fitness such as functional well-being and general health, but may have less of an impact on a subscale like emotional well-being. As an example, Galvao (2006) found that men with prostate cancer who were receiving androgen deprivation therapy and a RE program improved on several objective measures of physical functioning (e.g., chair rise to standing, 6m slow walk, 6m backwards walk, 400m walk, stair climb, and balance). Based on these findings

Table 3. Quality of life domains used in the medical outcomes survey.

MOS-SF36 QOL Domain	Meaning of Domain	
	Low	High
Physical Functioning	Limited a lot in performing all physical activities including bathing and dressing	Performs all types of physical activities including the most vigorous without limitations due to health
Role Physical	Problems with work or other daily activities as a result of physical health	No problems with work or other daily activities as a result of physical health
Social Functioning	Extreme and frequent interference with normal social activities due to physical and emotional problems	Performs normal social activities without interference due to physical or emotional problems weeks
Bodily Pain	Very severe and limiting pain	No pain or limitations due to pain
Mental Health	Feelings of nervousness and depression all of the time	Feels peaceful, happy, and calm all of the time
Emotional Role	Problems with work of other daily activities as a result of emotional problems	No problems with work or other daily activities as a result of emotional problems
Vitality	Feels tired and worn out all the time	Feels full of pep and energy all of the time
General Health	Believes personal health is poor and likely to get worse	Believes personal health is excellent

Note: MOS-SF36 = Medical Outcomes Survey: Short Form 36; QOL = Quality of Life. From Ware & Sherbourne, 1992 (p. 475)

Galvao (2006) noted that the reason why QOL may have improved in the Segal's study is because physical functioning (a component of QOL) improves through RE. Given the dearth of studies and different populations studied, it is possible that the different QOL

outcomes could be explained by yet unexplored participant characteristics (e.g., diagnosis, gender, importance placed on each QOL domain), study design and exercise prescription.

Fatigue.

Both Segal et al. (2003) and Courneya et al. (2007) measured fatigue using the FACT-F (fatigue specific QOL). In the study by Segal and colleagues, the men being treated for prostate cancer and given the intervention experienced a small improvement in fatigue of 0.8 points while the control group's fatigue worsened by 2.2 points, creating both a statistical and clinically significant difference between groups ($p < 0.01$); 3 points represents the minimal clinically important difference with the FACT-F (Cella, Eton, Lai, Peterman, & Merkel, 2002). Despite using a similar study design with a slightly higher training volume, Courneya et al. (2007) did not find meaningful reductions in fatigue in the RE group. As above, differences in cancer diagnoses, treatments, gender differences, and attendance (10.8% higher in the Segal study) could all account for the discrepancy between these studies.

Other benefits.

In addition to the fitness and QOL benefits associated with RE, Courneya et al. (2007) also found that RE led to faster completion of chemotherapy in breast cancer survivors by increasing the relative dose intensity compared to controls (mean difference = 5.7%, $p = 0.03$) (Courneya et al., 2007). There was no significant difference between those given an aerobic intervention and the controls in this study, suggesting improved chemotherapy completion may be a benefit unique to RE. Another benefit of RE observed in this study was a small but significant improvement in self-esteem (mean

change = 0.3, $p = 0.02$), that was also observed in the aerobic exercise group. Other outcomes, such as depression and anxiety, were positively influenced by the exercise interventions (both aerobic and RE) but did not reach statistical significance.

Adverse events and safety.

AEs were reported in two of the reviewed studies. Courneya et al. (2007) reported two AE's but noted that the events were unrelated to RE and occurred as a result of VO_2max testing (n = 2) and both participants recovered quickly (Courneya et al., 2007). Cunningham and colleagues (1986) noted that five participants from the exercise groups could not continue the study due to medical complications (pulmonary dysfunction n = 3, cardiomyopathy due to cyclophosphamide n = 1, and severe thrombocytopenia n = 1) but these events were not caused by the RE intervention. AE's were not reported by Segal et al. (2003) (n = 155) or by Galvao and colleagues (2006) (n = 10). Both of these studies noted that their intervention did not significantly elevate serum testosterone levels, which could interfere with the androgen deprivation therapy the participants were undergoing.

With no AEs being reported that resulted from RE, while preliminary, it appears that RE is safe and beneficial for those undergoing cancer treatment. However, this is only based on four studies that each sampled different cancer diagnoses. It is unknown if RE is safe for other groups of cancer survivors during treatment and the safety of RE in these groups needs to be confirmed in other studies. It has also not been adequately tested by these studies if intense RE interventions are safe since only Galvao and colleagues (2006) used resistances exceeding 70%1RM. One exception to this is a combined modality study that showed intensities between 70-100%1RM are well tolerated with proper monitoring procedures and precautions in place (such as excluding those with

brain or bone involvement) (Adamsen et al., 2009). More studies using different cancer diagnoses and exercise prescriptions are needed to provide a greater evidence base to support the safety of RE during cancer treatment.

Adherence to resistance exercise.

While the data are limited, early studies have shown that adherence to RE during cancer treatment is relatively high. For example, Segal et al. (2003) reported that of the 82 men randomized to an exercise group, only 8 (9.8%) dropped out of the study (drop out in the control group was 16.4%). Reasons for dropping out were not reported. Courneya et al. (2007) reported that out of the 82 women randomized to an RE group in their study, 26 (31.7%) did not complete 66% or more of the supervised exercise session; reasons for dropout were not given. Additionally, those in the RE group attended 68.2% of the offered sessions and were able to train at the prescribed level between 94.5-96.9% of the time. Barriers to exercise in this study were reported elsewhere (Courneya et al., 2008) and it was found that 53% of missed sessions were explained by disease or treatment related barriers. Only one participant from Galvao et al. (2006) dropped out of the study due to an unrelated respiratory infection and was not included in the analysis. Finally, Cunningham et al. (1986) reported that 4 out of the 10 participants (40%) randomized to three-times-a-week RE did not continue the study (refused to continue n = 1, medical complication n = 3), and that 4 of the 10 participants (40%) from the five-times-a-week RE group also dropped out (refused to continue n = 2, medical complication n = 2). Together, 142 of the 184 participants (77.2%) randomized to RE in these studies were able to adhere to their prescribed intervention.

Only the study of breast cancer survivors reported the long term adherence to the activity prescription (Courneya et al., 2009). Six months following the intervention 58% of the study's participants were meeting either aerobic or RE guidelines, compared to just 23% at baseline. Among other variables, it was found that muscular strength ($p < 0.01$) and increased strength over the course of the study ($p < 0.01$) were significant predictors of meeting exercise guidelines. Importantly, this finding suggests that RE programs that are designed to maximise strength gains may have a positive impact on long term adherence to exercise. Fatigue at the end of the study ($p = 0.03$), fatigue reduction during the study ($p = 0.03$), body mass index ($p = 0.03$), and percent body fat (%BF) ($p < 0.01$) also predicted adherence at six months and should also be maximised in RE programs.

Conclusions.

The greatest limitation in this area of research is the small number of studies that have provided RE to those receiving treatment for cancer. Moreover, direct comparisons between the studies cannot be made due to methodological differences (e.g., intervention protocols, outcome measures) and heterogeneity of the populations studied. However, this review suggests that there is promising evidence that RE during treatment can improve muscular fitness, body composition, fatigue symptoms, QOL, chemotherapy completion rates, self-esteem, and psychological well-being. This review also suggests that RE is safe for those undergoing cancer treatment and that adherence to RE during treatment is relatively high. Future studies are needed to better document the benefits of RE for survivors receiving treatment and should not be avoided due to concerns about safety or poor adherence. Given the dearth of data, future studies should continue to study survivors with a variety of diagnoses (especially gynecological cancers which are absent)

and demographic backgrounds to increase generalizability. Comparisons between RE prescriptions should be made to optimize benefits and inform exercise guidelines.

Resistance Exercise Following Treatment

Eight studies involving RE after treatment were identified (Table 4). Unlike RE during treatment, the bulk of the studies (n=6) have been conducted with survivors of breast cancer. The importance of this is that most of our understanding of how RE benefits survivors after treatment is based on studies of breast cancer survivors and is therefore is a logical point to begin studying optimal exercise prescription. Consistent with the previous section of this review the potential benefits of post-treatment RE will be presented along with safety considerations and adherence issues.

Muscular fitness.

Of the eight studies that are included in this section of the review, six included some measure of muscular fitness. In four studies, improvement in bench press strength ranged from ~12% to 63% and leg press improvements ranged from~20% to 39% (Musanti, 2012; Ohira, Schmitz, Ahmed, & Yee, 2006; Rajotte et al., 2012; Winters-Stone et al., 2012). There was significant improvement in strength an all studies compared to controls (all. $p \leq 0.04$). By far the most effective RE intervention in these four studies was the one offered by Schmitz and colleagues (Schmitz et al., 2005). This study used a relatively traditional RE protocol which included nine exercises done twice a week for three sets of 10-12 repetitions at 75-80%1RM (lower body) or symptom limited weight (upper body). The study also reported high attendance for the first six months of exercise (the control group was given the full program after six months) (Immediate treatment group = 92%; Delayed treatment group = 88%).

Table 4. Summary of randomized experimental trials after cancer treatment.

Study	Participants	Design	Length	Freq.	Sets/Reps	Intensity	Results
Kim et al., 2010	Breast (n=40‡)	2 Arm RCT RE No Exercise	8	5	2/10	0.5-1.0kg	↑ Role Physical QOL, General Health QOL ↓Proximal arm volume —Other QOL components
LaStayo et al., 2011	Cancer any stage (40‡)	2 Arm Pilot Eccentric RE No Exercise	12	3	3-5min progressing to 16-20min	RPE 7/20 progressing to 11-13/20	↑lean tissue mass in quadriceps, 6MWT ↓time to descend stairs —knee extension peak strength and power,
Lee et al., 2010	Breast (n=26‡)	3 Arm Pilot RE Shoulder Exercise Historic Controls	8	1	NR	NR	↑shoulder abduction & internal rotation ROM in shoulder, physical functioning ↓Fatigue —Arm disability, physical activity, QOL, shoulder ROM & strength in other directions

Study	Participants	Design	Length	Freq.	Sets/Reps	Intensity	Results
McKenzie & Kalda, 2003	Breast I, II (n=14 ‡)	2 Arm Pilot RE No Exercise	8	3	2/10 then 3/10 after first week	Light weight as tolerated	↑Physical functioning, general health, vitality – Other QOL components, arm volume
Musanti, 2012	Breast I-IIIb (55‡)	4 Arm RCT RE CE RE+CE Flexibility	12	3 (RE) or 2 (RE+AE)	1/10-12	RPE 3-5 out of 10 progressing to 7-8	↑Chest press 1RM, number of arm curl reps, shoulder abduction ROM, physical strength and attractive body (physical self-esteem components) ↓depression & anxiety
Ohira et al., 2005; Schmitz et al., 2005	Breast I-III (n=81 ‡)	2 Arm RCT RE Waitlist Controls	52	2	progressed to 3/10-12	0-0.5lb (upper body); 75-80%1RM (lower body)	↑chest press and leg press 1RM, LBM, Physical global score, Psychosocial global score ↓%BF, IGF-II – Glucose, Insulin, other IGF axis proteins

Study	Participants	Design	Length	Freq.	Sets/Reps	Intensity	Results
Rajotte et al., 2012	Cancer I-IV (187‡)	Pre-Post	12	2	individualized	individualized	↑6MWT, bench press & leg press 1RM, ROM, QOL ↓body pain, musculoskeletal symptoms, fatigue, insomnia, blood pressure – Resting heart rate, weight, waist circumference, cramps
Winters-Stone et al., 2011; Winters-Stone et al., 2012	Breast I-IIIa (106‡)	2 Arm RCT RE Flexibility	52	3	1-3/8-12	60-80%1RM	↑Bench press & Leg press 1RM, LBM, ↓serum deoxypyridinoline – Osteoclacin, Bone mineral density – Fat mass or %BF, timed chair stands, walking gait, standing balance, fatigue, Physical Function

Note: Length = intervention length weeks, Freq = Training frequency in days/week. RCT = randomized controlled trial. RE = resistance exercise. CE = cardiovascular exercise. 1RM = one-repetition maximum, LBM. = lean body mass. QOL = quality of life. RPE = ratings of perceived exertion. 6MWT = 6 minute walk test. ROM = range of motion. IGF = insulin-like growth factor. %BF = percent body fat.
↑increase
↓decrease
– No change

Two of the reviewed studies measured muscular fitness with isokinetic dynamometers (LaStayo, Marcus, Dibble, Smith, & Beck, 2011; Lee et al., 2010) and neither was able to show that their interventions improved muscular strength. In the first study, LaStayo and colleagues found that an experimental group doing 12 weeks of eccentric exercise on a recumbent stepper increased voluntary knee extension peak force by 11%. Yet this did not reach statistical significance compared to the control group who only had an increase in peak force of 1%. ($p = 0.15$). In the second study, Lee and colleagues were able to demonstrate that a shoulder mobility program, which primarily included light upper body exercises with stretching, was superior to traditional RE and historical controls for improving performance in an isokinetic test of external rotation ($p < 0.01$). It is likely that traditional RE was not superior to the shoulder mobility program in this case because it was not as specific as the shoulder mobility program (which included 14 scapula-oriented exercises) to the type of testing that occurred. While a targeted shoulder mobility program may be superior to traditional RE for improving shoulder strength, it is important to keep in mind that other benefits of RE such as improvements in lower body strength and improvements in lean body mass may not occur. These last two studies suggest that non-traditional forms of RE, such as eccentric stepping and targeted rehabilitation techniques, may also have a level of success in improving muscular strength and could have a unique place in cancer rehabilitation.

Body composition.

Many of the RE studies (n = 5) after treatment included some measure of body composition as an outcome. The most common measures of body composition were LBM and %BF. These outcomes are particularly important as they have been shown to

relate to other health problems, such as osteoporosis and cardiovascular disease (McTiernan, 2004); which many survivors are already at an increased risk of developing (Brown, Brauner, & Minnotte, 1993; Hewitt et al., 2003; McTiernan, 2004; Winters-Stone et al., 2011; Winters-Stone et al., 2012).

Three studies included LBM as an outcome and each of them reported significant increases following RE. Schmitz and colleagues (2005) reported increases of LBM of 0.88±0.23kg ($p < 0.01$) that were significantly correlated with QOL outcomes including general, physical, and psychosocial QOL (Ohira et al., 2006). A second study (Winters-Stone et al., 2011) found that within the RE group those breast cancer survivors who were also using aromatase inhibitors significantly increased LBM compared to those in the group not using them ($p < 0.01$), the authors speculated that aromatase inhibitors (drugs that block the production of estrogen) may act synergistically with RE to improve LBM. One last study (LaStayo et al., 2011), showed that eccentric RE on a recumbent stepper increased the lean tissue in the quadriceps by 1.7cm^2 compared to controls who lost 0.1cm^2 ($p < 0.01$). Together, these studies suggest RE after treatment can increase LBM.

Unlike changes in LBM, there is little evidence to suggest that RE on its own can reduce %BF in survivors and this also seems true for other measures of body fat such as waist circumference. In fact, only one study (Schmitz et al., 2005) reported a significant change in %BF (-1.15%, $p = 0.03$), although there was no change in total body weight in this study. Three other studies measured this outcome and found no change in whole body fat mass (Musanti, 2012), %BF (Winters-Stone et al., 2011), body weight, or waist circumference (Rajotte et al., 2012). These studies suggest that RE is ineffective at

managing the weight gain that some survivors experience. Other interventions, such as aerobics and diet control may be better alternatives for survivors hoping to decrease body fat. Therefore, a complete approach to managing the side-effects of cancer and its treatments should combine RE with aerobics and nutritional counselling to increase LBM while lowering %BF.

Quality of life.

QOL was another outcome included in most studies with six studies reporting the effects RE had on QOL. Five of these studies found that their RE interventions significantly improved at least one component of QOL. As anticipated, the most common benefit of RE on QOL was the improvement in the physical domains (i.e., aspects of QOL that relate directly to the health and function of the body). Specifically, three studies found RE significantly improved physical functioning and general health using the Medical Outcome Survey – Short Form (MOS-SF36; (Ware & Sherbourne, 1992) (Kim et al., 2010; McKenzie & Kalda, 2003; Rajotte et al., 2012) while a fourth study (Ohira et al., 2006) reported an improvement in the physical global score of the Cancer Rehabilitation Evaluation System (Schag, Ganz, & Heinrich, 1991) ($p < 0.01$). This is likely because improvements in fitness lead to improvements in the physical domains of QOL as suggested by correlations between the physical global score and bench press 1RM ($r = 0.32$, $p < 0.01$) and physical global score and LBM ($r = 0.23$, $p < 0.05$) (Ohira et al., 2006).

Until recently, improvements in physical functioning have only been shown in subscales of QOL questionnaires, which are subject to the limits of that measurement technique such as self-report bias. Three recent studies included objective measures of

physical functioning by including physical tasks such as sit-to-stand and timed stair climbing. Results of these studies are mixed, with two showing RE was beneficial (LaStayo et al., 2011; Rajotte et al., 2012) and one showing no significant improvement (Winters-Stone et al., 2012). Because of the mixed results using functional tasks it may become more necessary for future studies to include objective measures of physical functioning.

It has also been shown that there are benefits to the psychosocial aspects of QOL, although these trends are less consistent. Four studies reported improvements in psychosocial aspects of QOL. First, Ohira et al. (2006) observed improvements in the Cancer Rehabilitation Evaluation System psychosocial global score in their RE group of their study compared to a decrease in their control group ($p = 0.02$). Similarly, Rajotte (2012) found that all components of QOL on the MOS-SF36 improved ($p \leq 0.02$). The results of these two studies are quite different from those results reported by Kim and colleagues (2010) who found that the only psychosocial component of QOL to significantly improve in their study was mental health, which did not translate to a significant difference when compared to the controls which experienced a similar improvement. Lastly, Lee (2010) found that the only psychosocial aspect of QOL to improve in their study was social functioning, and this was seen in the shoulder mobility group and not the RE group.

It is likely that psychosocial aspects of QOL are not achieved through improvements in fitness alone. Rather, it is much more likely that these outcomes are achieved when groups of survivors come together for exercise and are able to develop a sense of togetherness through positive group dynamics (Adamsen, Rasmussen, &

Pedersen, 2001; Emslie et al., 2007; Midtgaard, Rorth, Stelter, & Adamsen, 2006). In this way, group exercise of any kind serves as a forum for survivors to forge friendships and share a common experience that few people can relate to. This develops an important social network for the survivors which can aid in coping and fosters positive feelings. Thus, it is not surprising that the two studies that reported the greatest improvements in psychosocial QOL offered their interventions in a group format (Ohira et al., 2006; Rajotte et al., 2012). The two studies reporting the least improvement do not specify whether or not exercise took part in a group or was done individually (Kim et al., 2010; Lee et al., 2010).

Only one study failed to report any improvements in QOL following the intervention (Winters-Stone et al., 2012). This study's inability to find significance may be due to two reasons. First, the study only examined the physical functioning scale of the MOS 36-SF and improvements in other QOL components may not have been identified. Second, while the study's intervention lead to small (yet statistically significant) improvements in muscular strength when compared to other RE studies, it is possible that these improvements were not enough to cause a perceived benefit in overall physical functioning. This is interesting from an exercise prescription standpoint because the RE protocol of this study was remarkably similar to the very successful program described by Schmitz et al. (2005) with the only major deviation being a reduction in training volume.

Fatigue.

Given the physiological and psychological toll of treatment, it has been suggested that the optimal time to begin an exercise program to improve fatigue is post-treatment

(McNeely et al., 2006). This claim was based on a review of exercise studies in breast cancer survivors, however there was only one study of RE included in this review. Within the current review, several additional limitations must be considered. First, few of the studies measuring fatigue as an outcome used the same questionnaire, again making direct comparisons difficult to make. Also, it is important to keep in mind that only survivors who are fatigued have the potential to reduce fatigue. This was demonstrated by Musanti (2012) who observed significant reductions in survivors with clinically significant fatigue (Cohen's $d = 1.5$, $p < 0.01$) but not in those without fatigue (Cohen's $d = 0$, $p = 0.99$). However, given the prevalence of fatigue, it was not surprising to find that six of the eight studies examined this outcome.

Regrettably, the findings about the efficacy of exercise on fatigue are mixed, with four studies showing a benefit and two showing no difference compared to controls. Of those studies that showed a benefit, two used subscales of their QOL inventories to indirectly assess fatigue. One found that following RE there was a significant improvement in MOS-SF36 vitality (thought to be the opposite of fatigue) ($p = 0.02$), but did not report fatigue scores at baseline (McKenzie & Kalda, 2003). The other study found that their RE intervention significantly reduced fatigue scores on the European Organization for Research and Treatment of Cancer questionnaire ($p = 0.03$) (Lee et al., 2010). This finding should be considered in the context that there was a non-significant trend towards the RE group being more fatigued than both the control group and shoulder mobility group ($p = 0.16$), and that following the intervention scores between groups were similar. Viewed from this perspective, it is difficult to conclude that the RE was truly a superior method for reducing fatigue in this study as it is possible the other groups

were not fatigued enough to experience a benefit. One last study, reported a reduction in fatigue symptom inventory scores from 1.68 to 2.47 (Cohen's $d = 0.52$, $p < 0.01$) and less insomnia (Cohen's d 0.40, $p < 0.01$ (Rajotte et al., 2012). Studies that have shown a benefit suggest meaningful improvements in fatigue may occur.

For those studies that found no benefit in fatigue symptoms, Kim et al. (2010) reported that RE did not improve MOS-SF36 vitality scores. However, the average fatigue score in this study at baseline was low, suggesting that fatigue was not a substantial concern for most of the study participants. The second study (Winters-Stone et al., 2012), which was a large randomized controlled trial (RCT) with 106 breast cancer survivors, also found no improvement in fatigue after 12 months of RE with the Schwartz cancer fatigue scale. Again, baseline scores indicated that high levels of fatigue were not common in this study's sample.

Taken altogether, there is early evidence that suggests RE may be able to relieve some level of fatigue in cancer survivors following treatment provided that high enough levels of baseline fatigue are present. More studies are needed to determine the full extent to which RE can help, as most of the studies detailed above have not targeted fatigued participants. These future projects may plan to exclude participants who are not clinically fatigued, stratify groups on baseline levels, or perform covariate analysis to prevent this limitation from occurring. Future studies should also determine which of the fatigue questionnaires is best for the purpose of measuring fatigue in survivors in exercise studies. Such a study would promote a more standardized approach to measuring fatigue in later exercise trials and would strengthen comparisons between these studies. Lastly, there was considerable variation in the effectiveness of the interventions in these six

studies. While baseline fatigue is clearly influencing this, it is also likely that the interventions themselves contribute to how much fatigue is relieved.

Other benefits.

Due to a combination of cancer, cancer treatment, and lifestyle changes, survivors of cancer are at an increased risk for future health problems including: cancer recurrence, cardiovascular disease, osteoporosis, and mental health issues (Brown et al., 1993; Costanzo, Ryff, & Singer, 2009; Hewitt et al., 2003). While there remains a relative lack of study, preliminary evidence is available to suggest that, like aerobic exercise, RE may confer specific short and long-term health benefits to survivors. Some benefits that have been observed are: 1) reductions in serum insulin-like growth factor II which relates to prevention of recurrent disease (Schmitz et al., 2005); 2) decreases in systolic and diastolic blood pressure which relate to cardiovascular disease (Rajotte et al., 2012); 3) preservation of bone mass in the lumbar spine and positive effects on deoxypyridinoline and osteoclacin levels which will slow down the development of osteoporosis (Winters-Stone et al., 2011); and 4) increases in self-esteem and decreases in depression and anxiety (Musanti, 2012). Although additional study is needed, the current evidence indicates that RE could help protect survivors from a wide variety of health problems.

Lymphedema is another common side-effect of breast cancer surgery that causes painful swelling of the arms and limits mobility and the ability to function. It has long been speculated this is made worse by RE. However, studies have shown that RE does not exacerbate symptoms (McKenzie & Kalda, 2003), and may even reduce swelling (Kim et al., 2010). Upper body mobility has been studied in relation to lymphedema and it has been shown that traditional RE significantly improved shoulder range of motion

(abduction, internal rotation, and external rotation) (Lee et al., 2010; Musanti, 2012). This may be because skeletal muscle does stretch during resistance exercises that move through a complete range of motion. These studies help debunk the myth that RE will exacerbate lymphedema in breast cancer survivors and help promote RE as a possible management strategy.

Adverse events and safety.

Two studies failed to report whether or not AEs occurred (Kim et al., 2010; McKenzie & Kalda, 2003). Two studies with a total of 146 participants reported that the RE intervention did not cause any AEs (LaStayo et al., 2011; Winters-Stone et al., 2011; Winters-Stone et al., 2012), although one of these studies (LaStayo et al., 2011) reported that five cases of unrelated illnesses occurred during the study. In the remaining four studies (Lee et al., 2010; Musanti, 2012; Rajotte et al., 2012; Schmitz et al., 2005) (n = 347) a total of 27 intervention related AEs were reported, indicating the approximate risk of an AE occurring to be low (approximately 5.5%)[2]. The overwhelming majority of AEs that did occur were minor musculoskeletal injuries that did not have any long lasting effects or impeded exercise (25/27 = 92.3%). These injuries included muscle soreness, tendinitis, and aggravation of existing injuries. Importantly, participants were able to continue exercising with modifications made to their programs such as lower intensity or volume. The more serious AEs included a pulled back muscle (Rajotte et al., 2012) and a wrist injury (Schmitz et al., 2005). The back injury was reported to have still affected the survivor at the end of the 12 week program while the wrist injury prevented the survivor from continuing exercise and was becoming worse over time. Specific mechanisms of

[2] 494 total participants divided by 27 AEs = 5.48%

injury, such as lifting more weight than was prescribed or improper lifting technique, were not reported. Because of the very low probability of these more serious AE occurring due to participation in RE (less than 1%), this review can only conclude that RE is safe which is in agreement with a recent review by Jones (2011).

Adherence to resistance exercise.

Similar to RE during treatment, dropout rates to RE after treatment appears to be low, ranging from ~15-24% (Musanti, 2012; Schmitz et al., 2005; Winters-Stone et al., 2012). The most common reasons for participant withdraw was being "too busy" to participate. Dropouts have been shown in these studies to share a number of common traits. These traits include: being closer in time to their cancer diagnosis, having lower mental health, and greater difficulty completing activities of daily living (Winters-Stone et al., 2012); they are also more likely to have severe fatigue, be obese, and be less physically active (Musanti, 2012). This is particularly troubling as it shows that those survivors who have the most to gain from RE are also the ones less likely to adhere to a program. This presents a challenge to health care professionals as strategies to promote adherence may include modifying the intervention, yet there have not been any studies to indicate which modifications are best to make. Future studies that compare different interventions are needed to inform how RE can be tailored for survivors who struggle with adherence.

Attendance was also reported to be high for sessions of supervised exercise and ranges from 76% to 95%, but was much lower for home-based exercise sessions at 23% which was a part of one intervention (Winters-Stone et al., 2012). Most studies were short term interventions ranging from 8 to 12 weeks in duration. However, there were

two longer studies which ran for one year (Schmitz et al., 2005; Winters-Stone et al., 2012). Both the study by Schmitz and colleagues and Winter-Stone and colleagues reported attendance for the first six months (92% and 82% respectively) and from months 6 to 12 (66% and 62%), and indicate that attendance can drop as much as 30% over the course of a year. This finding is not unexpected as a similar trend exists in the general population. As it is apparent that many survivors have difficulty maintaining RE in the long term and risk becoming inactive, long-term adherence strategies will need to be developed. Studies that follow-up on participants or provide longer interventions (up to a year) can help in this area.

Attendance was often used as an indicator of compliance (the degree to which the intervention was followed), in these studies compliance to the intervention was high. Compliance remained high even when other operational definitions of compliance were used. For example, Winters-Stone (2011) reported excellent compliance (98%) which was defined as the percentage of participants who completed the study without significant modifications for six months.

Overall, it appears that most cancer survivors are able to adhere to a RE program, although some types of survivors will have a more difficult time maintaining RE than others. Strategies will need to be developed to support these individuals as well as any survivor hoping to maintain exercise longer than six months. Strategies such as modifying the exercise prescription or building the intervention around a theoretical framework, such as self-determination theory, may be helpful (Milne, Wallman, Guilfoyle, Gordon, & Corneya, 2008; Perri et al., 2002).

Conclusions.

Several general statements about RE after cancer treatment can be made upon reviewing the available literature. First, RE is beneficial for survivors and is likely to result in improvements in muscular fitness, LBM, and QOL (especially physical functioning). Positive changes in fatigue symptoms (if this is a problem for the individual) and protection from other health problems such as recurrent cancer, cardiovascular disease, and osteoporosis may also occur. The risk of harm resulting from RE is low and most all injuries (99%) appear to be minor, easily recovered from and not preventing a survivor from continuing exercise. It is also expected that most survivors will be able to adhere to a RE program for at least six months, although some survivors may have greater difficultly doing this than others.

Future research is needed for other survivor groups since the majority of RE studies done post treatment used groups of breast cancer survivors. Additionally, more studies are needed that directly compare different RE regimens. It is entirely possible that certain RE programs are more beneficial than others and such comparisons will allow superior RE interventions to be made.

Exercise Prescription

In order to effectively provide sound guidelines for a particular population, including cancer survivors, training principles and variables need to be carefully considered. Training principles may be thought of as generalized guidelines founded in exercise physiology. For example, (Heyward & Gibson, 2014), describes seven basic training principles (see Table 5). Training variables, on the other hand, are those variables which are specified in a training program to satisfy the training principles. For example,

if the desired outcome of a training program is an increase in muscular endurance than the training variables should reflect this (e.g., low weight, high repetitions, minimal rest). There are numerous examples of training variables in order to reflect the plethora of physical activities one may engage, but they are most often simplified using the FITT format (frequency, intensity, time, and type). However, it is this author's opinion that when describing RE, it may be more useful to describe exercise in terms of frequency, intensity, volume. As these variables are discussed further, they will be related back to training principles.

Table 5. Seven training principles.

Training Principle	Description
Specificity of Training	Adaptations to exercise are specific to the demands placed on specific muscle groups
Overload	Adaptations occur when physiologic systems are taxed by demands they are not yet accustomed to
Progression	Gradual progression is needed for continued adaptation to exercise
Initial Values	Those with low initial fitness show faster adaptation to exercise than those with high initial fitness
Diminishing Returns	As adaptations approach an individual's genetic limit, improvements occur more slowly
Reversibility	The benefits of regular physical activity are lost after a period of time without exercise (detraining)

Note: Based on training principles in Heyward &Gibson (2010).

Intensity.

Strictly speaking, training intensity is the amount of effort required to perform a specific exercise (ACSM, 2013). It may also be considered as the rate of energy expenditure for a given exercise. For example, running faster or lifting heavier weights,

both examples of increased intensity, require a greater energy output per unit of time. Regardless, in the context of RE, intensity may be expressed multiple ways (Fry, 2004) including: the absolute amount of weight lifted (pounds or kilograms), as a percentage of a maximum lift (%1RM), the number of repetitions that can be completed before failure (repetition maximum or RM), or using the Borg Scale of Perceived Exertion (Borg, 1982). In RE, intensity is inversely related to the number of repetitions that may be performed in a given set (Brzycki, 1993). Because the number of repetitions one can perform is so closely related to training intensity they are discussed here and not with training volume (the number of sets and exercises).

The importance of training intensity relates mainly to the principle of specificity. Due to the inverse relationship between the amount of effort needed to perform a lift and the number of repetitions that may be performed, intensity based training zones may be categorized as: High Intensity Low Volume (HILV), Moderate Intensity Moderate Volume (MIMV), and Low Intensity High Volume (LIHV). Although some adaptations to RE are common to these training zones including shifts from type IIB to Type IIAB muscle fibers and myosin heavy chain (MHC) shifts from MHCIIb to MHCIIa; each of these training zones has been shown to bring about specific physiologic adaptions that affect performance in unique ways following the principle of specificity (Table 6) (Campos et al., 2002).

HILV training, which uses loads corresponding to 80%1RM and heavier, have been shown to be the most efficient at increasing strength (average force production) (Campos et al., 2002). Physiologic adaptations to this kind of training include: increased

cross sectional area of muscle fibers (myofibular hypertrophy) (Campos et al., 2002), increased neural drive such as increased recruitment of motor-units, faster firing rates, and better coordination (Häkkinen, Alen, & Komi, 1985; McArdle, Katch, & Katch, 2010), and elevated levels of testosterone (Raastad, Bjøro, & Hallen, 2000).

MIMV training is often described as ranging from 85-70%1RM. This training zone is mostly associated with increased strength and muscle hypertrophy (Wernbom, Augustsson, & Thomeé, 2007) exhibiting both myofibrillar and sarcoplasmic hypertrophy (increases in non-contractile elements and fluid in muscle) (Fry, 2004). Evidence for sarcoplasmic hypertrophy and its association with MIMV training comes from comparisons between power lifters and bodybuilders and their different training methods (Fry, 2004; Schoenfeld, 2010). Power lifters typically train using very high intensity lifts and low volume (e.g., 95%1RM) while body builders train using moderate intensities for higher volumes (70-85%1RM). In comparison to power lifters, bodybuilders have more fibrous endomysial connective tissue and higher muscle glycogen content (Schoenfeld, 2010) and display hypertrophy of both type I and type II fibers while only type II fibers are hypertrophied in power lifters (Fry, 2004). Additionally, MIMV training also has the unique adaptation of increased capillaries per area for type IIA muscle fibers (Campos et al., 2002).

Lastly, LIHV training which is less than 70%1RM, and primarily increases muscular endurance (Campos et al., 2002). Physiologic adaptions include increases in aerobic power and time to exhaustion in aerobic fitness tests (Campos et al., 2002). Additionally, LIHV training also appears to be associated with higher levels of human growth hormone and cortisol responses which may be useful for enhancing the hormonal

response when primarily training with other intensities (Kraemer & Ratamess, 2004)(Kraemer & Ratamess, 2005).

Table 6. Summary of specific adaptations to strength training intensity zones.

Adaptations	HILV (100-80%1RM)	MIMV (85-70%1RM)	LIHV (≤70%1RM)
Fitness Tests			
1RM	↑↑↑	↑↑	↑
Standard Load Test (60%1RM)	↑	↑	↑↑↑
Aerobic Capacity (VO_2max)	-	-	-
Time to Fatigue	-	-	↑
Aerobic Power	-	-	↑↑
Fiber Type Distribution			
IIB (%)	↓	↓	↓
IIAB(%)	↑	↑	↑
MHCIIb	↓	↓	↓
MHCIIa	↑	↑	↑
Hypertrophy			
Type I	↑	↑↑	-
Type IIA	↑↑	↑↑	-
Type IIB	↑↑	↑↑	-
Sarcoplasmic	-	↑	-
Capillarization			
Capillaries/area	-	-	-
Capillaries/fiber type	-	↑ (type IIA)	-
Neural Drive	↑↑	↑	↑
Hormonal			
Testosterone	↑↑↑	↑↑	↑
Human Growth Factor	↑	↑↑	↑↑↑
Cortisol	↑↑	↑↑	↑↑↑

Note: HILV = High Intensity Low Volume; MIMV = Moderate Intensity Moderate Volume; LILV = Low Intensity Low Volume; 1RM = one repetition maximum; MHC = myosin heavy chain.
- No Change
↑Small increase
↑↑Moderate increase
↑↑↑Large increase

Training experience may also be an important consideration when selecting an appropriate training intensity. One meta-analysis found optimal intensity for individuals with less than one year of experience to be 60%1RM vs 80%1RM for experienced weightlifters (Rhea, Alvar, Burkett, & Ball, 2003). Second, while studies specifically comparing training intensity in cancer survivors are not yet published (Buffart et al., 2014), one study of healthy postmenopausal women found that high intensity training (80%1RM) was only superior to low intensity (40%1RM) for improving upper body strength with no differences in overall strength improvements (averaged across 13 exercises), cross sectional area of biceps brachii or rectus femoris, or bone mineral density (Bemben, Fetters, Bemben, Nabavi, & Koh, 2000). Taken together, these studies suggest that for the typical breast or gynecologic cancer survivor who is not strength training, high intensity may have limited value. For this reason, a training zone of 10-14RM (approximating 65-75% of 1RM) was chosen for the main study.

Training volume.

Training volume is defined as the total amount of work done for a given bout of exercise. As such, strength training volume is predominantly affected by the number of sets and repetitions of a given exercise or related exercises, however, intensity (discussed previously) also factors into the equation (Feigenbaum & Pollock, 1999). As mentioned a good guideline for selecting a repetition range is to base it on training intensity to bring about the desired adaptations based on training specificity. Therefore, this discussion on training volume will focus on the number of sets that should be performed.

The exercise prescription literature appears divided on what constitutes optimal training in regard to the number of sets that should be performed for each exercise (Rhea,

Alvar, & Burkett, 2002). There is support for one set protocols (Carpinelli & Otto, 1999; Feigenbaum & Pollock, 1999). For example, in a review of eight studies comparing single versus multi-set protocols, Feignbaum and Pollock found that only one report showed a small (2.9%) but significant benefit for multiple training sets (Berger, 1962). A meaningful benefit of single set protocols are findings that suggest that adherence may be better due to lower time commitments. Depending on the number of exercises performed, a single set program may only take 20 minutes to complete versus 50 minutes using three sets (Messier & Dill, 1985). For cancer survivors, it is often cited that a lack of time is one of the main reasons for poor adherence in exercise trials (Courneya et al., 2005; Rogers et al., 2007) so if effective single set protocols may be preferred.

Those who are not in favor of single-set programs point to limitations in research that have shown no significant differences in strength development. Rhea and colleagues (2003), for example, have shown that many studies that do not demonstrate a difference between single and multi-set protocols are often underpowered due to small sample sizes and are potentially committing a type II error. In order to make the results from previous studies clearer, a meta-analysis was performed pooling the results of 16 studies directly comparing one set against three set protocols (total participants n = 93). From this, it was found that three sets lead to greater improvements in strength than single set protocols (*ES* = 0.23). These results were robust and remained significant between trained (*ES* = 0.55) and untrained individuals (*ES* = 0.25), and were strengthened in sub-analysis of studies which controlled for other training variables such as intensity. These authors speculate that part of the confusion between single versus multiple sets is that studies supporting single sets often use multiple exercises for the same muscle group (i.e., squat,

leg press, and leg extension) meaning they are not truly single set protocols. In a follow-up meta-analysis of optimal exercise prescription it was also found that an optimal strength training program for healthy untrained individuals is four sets of 60% of 1RM done twice weekly (Rhea et al., 2003).

More recently, the literature of single versus multiple sets was re-examined focusing on studies published after 1998; the year in which Carpinelli & Otto (1998) published a review paper supporting single sets (Galvao & Taaffe, 2004). Unlike the previous review, which only found one study in support of multiple sets, 7 out of 8 modern studies support multiple set protocols. This included both short (≤12 weeks) and long term (>12 weeks) studies using both trained and untrained participants. These results are quite robust and are supported by additional arguments related to increased testosterone production with additional sets.

To date, single versus multiple sets remains controversial even when considering healthy populations, and no data are available to support either side in regard to survivor populations. One study examined single vs. multiple sets in previously trained post-menopausal women with osteopenia which may generalize to breast and gynecologic cancer survivors (Kemmler, Lauber, Engelke, & Weineck, 2004). In this study, single sets were compared to multiple sets (2-4 sets) in post-menopausal women who had already completed 18 months of aerobic and resistance training using a crossover design. In this study, significant differences were realized in 1RM strength in leg press, bench press, rowing, and leg adduction between the two protocols in favor of multiple sets. One limitation is that these results may not generalize to untrained cancer survivors due to the previous training received by participants in this study.

Considering the evidence presented by both sides of the single versus multiple set controversy an initial training volume of two sets for cancer survivors appears to be an ideal way to balance the need for additional sets without overburdening survivors. As mentioned, the evidence supporting multiple sets is robust and comes from modern studies, and is supported by two meta-analyses (Rhea et al., 2002; Rhea et al., 2003). While compelling, this evidence does need to be weighed against the increased time commitment of multiple sets, especially given the adherence barriers reported by cancer survivors (Rogers et al., 2007). Based on the times needed to complete one and three sets reported by Messier & Dill (1985), survivors should be able to complete two sets of major exercises in approximately 40 minutes (one set was reported to only take 20 minutes to complete) which may still represent a minimal time commitment for most survivors.

Training frequency.

The issue of training frequency is centered around providing the body sufficient time to recover from and adapt to exercise. Providing too much time allows deconditioning to take place, while providing too little time may result in over-training and/or over-reaching. During a bout of exercise as energy stores are depleted and the musculoskeletal system experiences micro-trauma causing soreness, performance declines (strength, power, speed, endurance, etc.). Following the bout of exercise recovery begins and the rate of muscle protein synthesis increases for a period of time, up to 50% 4 hours post exercise and 110% 24 hours post-exercise (Chesley, MacDougall, Tarnopolsky, Atkinson, & Smith, 1992). Increases in fitness occur when recovery processes overshoot the individual's baseline fitness to adapt to the physical stressor that

was experienced. If the individual exercises again using a progressively challenging protocol, the net effect of this process repeating over time will be positive and further increases in performance.

While the American College of Sports Medicine (ACSM) guidelines recommend at least 48 hours recovery following resistance exercise (ACSM, 2013), training frequency appears to depend on numerous variables. For example, weightlifters and bodybuilders need to train 8-12 times/week (using double split routines) in order to see continued improvement (Kraemer & Ratamess, 2004) while those with very low fitness may still benefit from one session each week (Heyward & Gibson, 2014). Clearly a very wide range of effective frequencies exist depending on factors such as training experience, intensity and volume of training sessions, nutritional status, age, and goals (Kraemer & Ratamess, 2004).

Several studies have been published to help explain the physiologic factors affecting training frequency. Studies comparing strength trained with non-strength trained individuals show that chronic strength training leads to increased mRNA activity coding for protein kinases (PDK4) and myogenic proteins (MyoD) (Coffey et al., 2006), and increased synthesis of protein (Chesley et al., 1992; MacDougall, Tarnopolsky, Chesley, & Atkinson, 1992). In elderly men (70 ± 5 years) protein synthesis has been found to be ~30% slower than their younger counterparts (age = 24 ± 6 years) (Kumar et al., 2009). The authors of this study described this as anabolic resistance and speculated that there is a blunted response to strength training which utilizes more type II fibers that are atrophied in older adults due to sarcopenia. If this is the case, there is little reason to

expect that females would not experience anabolic resistance with age until this study is repeated with female participants.

Physiologic variables aside, training frequency should also be considered with an individuals' schedule in mind (ACSM, 2013). This is particularly important for cancer survivors for whom time is frequently cited as a barrier to exercise (Courneya et al., 2005; Rogers et al., 2007). In a practical setting, individuals who do not have enough time to commit to whole body training may be able to use split routines (training some muscle groups one day and the other muscle groups on another) (ACSM, 2013). There is also anecdotal evidence that using split routines may have an added benefit of limiting the physical and mental fatigue of long training sessions which may be particularly beneficial for fatigued survivors. Another time saving technique is circuit training, where one muscle group is trained while another rests (e.g., after completing a set of bench presses a set of leg press is done rather than resting. To date, no study has compared the benefits of these techniques against other programs.

Because the typical cancer survivor is older, often with limited RE experience, and limited time available for training, low training frequencies (1 or 2 days per week) appear to be the most appropriate. Cunningham et al. (1986), found no increase in arm muscle area or differences between groups of leukemia patients training 3 for 5 times per week. This study used a relatively high training frequency, yet other studies using lower frequencies have found more benefit (Courneya et al., 2007; Galvao et al., 2006; Segel et al., 2003), albeit differences in measures (arm volumes versus 1RMs) and timing of the intervention (during cancer treatment versus after) may have limited the Cunningham study's ability to find meaningful improvements for survivors. Studies re-examining

training frequency are warranted to establish its benefits which may lead to better adherence rates and make rehabilitation programs more feasible from a cost-benefit perspective.

Resistance Exercise Guidelines and Recommendations for Survivors

As survivorship of cancer has continually been increasing there has been an increased demand to provide methods for controlling the long term side-effects of cancer and its treatments. While numerous studies, reviews, and meta-analyses are available demonstrating that exercise, including RE, is an effective solution to these problems, the provision of a strong evidence-base for RE guidelines is lacking. Although recommendations are available (Table 1) (Courneya et al., 2002; Courneya et al., 2004; Durst, 2009; Galvao & Newton, 2005; Lucia, Earnest, & Perez, 2003; Schmitz et al., 2010; Smith, 1996), their relative lack of consistency ultimately provides a vague RE prescription that is of little use (one to three sets of 3-15 repetitions at intensities ranging from 40-80%1RM, or very light to light weights; done one to three times-a-week). When the issue of progression is addressed it was often recommended to progress in "small increments".

The lack of specificity of the existing guidelines and tailored RE recommendations is particularly problematic because the uncertainty it creates often becomes a barrier to promoting RE to survivors. When one considers the unique benefits RE has for survivors that have been discussed in the previous sections, this becomes especially troubling. Nevertheless, it is important to keep in mind that existing guidelines are still useful for survivors and oncologists making general RE recommendations for those in their care. Physical activity recommendations help protect survivors from the

consequences of becoming inactive, such as muscle atrophy and bone loss (Schwartz, 2008), and may also lead to positive health benefits including increased muscular fitness and QOL. What follows is a discussion of available RE guidelines that would be applicable to those with breast cancer and the evidence used to develop them, limitations of the guidelines, and recommendations for future research. A discussion of gynecologic cancer exercise guidelines would be limited as only one set of guidelines are available (Schmitz et al., 2010) and those recommendations are said to be identical to those for the general population with more caution given if there is an active health problem related to cancer treatment.

Resistance Exercise Guidelines and Quality of Evidence.

Recently the available exercise recommendations for those with cancer were reviewed (Humpel & Iverson, 2005). In their search of available literature they reported finding seven journal articles that made specific recommendations for exercise prescription for those with cancer. Of these seven, three did not provide any RE specific suggestions (Courneya, Mackey, & Jones, 2000; Drouin & Pfalzer, 2001; Winningham, 1991); two provided prescriptions that lacked details related to either frequency, volume (Smith, 1996), or intensity (Lucia et al., 2003); and two provided complete exercise prescriptions (Courneya et al., 2002; Courneya et al., 2004). It is worth noting that only one set of guidelines was specific to breast cancer (Courneya et al., 2002) while the remaining six were deemed suitable for all diagnoses.

Humpel and Iverson (2005) also reviewed the quality of the evidence that these guidelines were based on with the Agency of Healthcare Research Quality's levels of evidence scale (this scale considers the quality of study descriptions, sampling,

measurement, analysis, and interpretation). Focusing only on those studies which provided recommendations on RE, it was noted that these guidelines were not based on sufficient evidence. For example, Courneya et al. (2002) were only able to base their guidelines on correlational studies of physical activity and cancer outcomes, one experimental study using a combined aerobic and RE intervention, and the available ACSM (Pollock et al., 1998) guidelines for healthy people. Additionally, one set of guidelines for older cancer survivors could only base its RE prescription on the ACSM guidelines due to the absence of studies using older cancer survivors (Courneya et al., 2004). Overall, Humpel and Iverson found the strength of evidence used to make exercise recommendations to be low.

Since the 2005 Humpel and Iverson review, other RE recommendations and guidelines have become available. These newer guidelines were able to be based on somewhat stronger evidence as more studies of RE in cancer survivors were published. (Galvao & Newton, 2005), made their RE recommendations based on seven studies of RE and RE plus aerobics (three during cancer treatment and four after). It was not specified if their resulting RE prescription was for survivors undergoing treatment or after treatment. It was also noted that many of the studies used to inform their guidelines did not adequately describe their exercise interventions. This appears to be a common issue as Schwartz (2008) reported that many of the studies used to inform her recommendations also failed to specify the dosage of exercise. Although Schwartz reviewed over 35 studies to develop these guidelines, specific justifications for her RE prescription are not given or how the recommendations were developed.

The two most recent guidelines have been provided by ACSM. First, in the latest edition of *ACSM's Exercise Management for Persons with Chronic Disease and Disability* there is a chapter about exercise for those with cancer (Durst, 2009). Here the benefits of exercise for survivors as well as information about exercise testing and prescription are detailed. The rationale that is given for the RE prescription is that low to moderate aerobic and RE is beneficial for those on treatment and that longitudinal studies show improvements in survivors with a variety of diagnoses. No specific studies are cited to support these claims, although the previous sections of this review suggest that low to moderate RE can improve some outcomes. It is also stated that information about optimal exercise prescription is not yet available and references to other guidelines are provided at the end of the book's chapter. No distinction is made about whether the ACSM guidelines are for those on or off treatment.

Finally, ACSM held a roundtable to discuss exercise prescription for those with cancer and recently published a consensus statement (Schmitz et al., 2010). Unlike many of the previous guidelines the literature review used to inform the current guidelines was based on the quality of the evidence provided for certain outcomes. It was found that the evidence for exercise improving muscular fitness in those with breast cancer was of the highest quality using the evidence ratings outlined by the National Heart, Lung, and Blood Institute, (Evidence level A = overwhelming data from randomized controlled trials; Evidence Level B = Few randomized controlled trials exist or they are small and results are inconsistent; Evidence Level C = results stem from uncontrolled, non-randomized trials, and/or observational studies; Evidence Level D = evidence insufficient for categories A to C) (NHLBI Obesity Education Initiative Expert, 1998). This was true

for both during and after treatment, although this outcome was based on a total of 11 studies (five during treatment and six after). Evidence for other outcomes such as QOL, body composition, and fatigue drew from both aerobic and RE studies and was usually evidence category B, meaning that few RCTs were available, and/or studies used small samples, and/or the results were inconsistent. No distinctions were made about whether the guidelines are for those on or off treatment.

Limitations.

While recommendations for RE have been proposed, overall there is a lack of understanding of RE within the cancer population to provide evidence-based, prescriptive advice. Moreover, several of the existing recommendations fail to make distinctions between survivors on and off treatment. Given the demands of treatment, it is likely that an optimal RE prescription would be different depending on the timing of treatment due to differences in exercise tolerance and motivation at these times (Humpel & Iverson, 2005; McTiernan, 2004). Additionally, it has been speculated that exercise may be more effective after treatment (Courneya et al., 2002; McTiernan, 2004). This may be due to better adherence, increased exercise tolerance allowing for more vigorous exercise, or recovery from cancer treatment.

A second limitation is that all of the recommendations presently available are at least partially based on studies which have combined RE with aerobics. This approach is used to include more studies in the development of guidelines and is justified by the notion that RE should be combined with aerobics to maximise health benefits for survivors. However, it is also a problem for research because it is difficult to separate the positive effects of aerobic exercise from the RE prescription. This makes it difficult to be

sure if the RE prescription was effective or if the positive changes in outcomes were due to the inclusion of an effective aerobic program.

Another issue is that several studies used in the development of these guidelines did not report all the details of their RE interventions, or used vague wording such as "very light weights" in the descriptions (Tables 2 and 4). Related to this, no study described the repetition velocity used in their intervention which may affect the development of different aspects of muscular fitness (Galvao & Newton, 2005; Pereira & Gomes, 2003). It has also been suggested that few of the studies have based their RE interventions on literature related to optimizing muscle hypertrophy and strength because few studies have used loads corresponding to 75-85% 1RM (Galvao & Newton, 2005). These resistances have been shown to be the most effective at enhancing muscular fitness (Kraemer & Ratamess, 2004; Kraemer et al., 2002). This may be due to safety considerations, however, it has been shown that intensities as high as 95% 1RM are well tolerated with proper monitoring (Adamsen et al., 2009).

An important strength of the current guideline is the recommendation that an individualized approach be taken with exercise prescription. While this advice is reasonable, it does become a practical issue since there is no evidence available to inform how to do this (Humpel & Iverson, 2005). For example, if a survivor becomes anemic should the intensity of exercise be lowered with a compensatory increase in training volume to potentially prevent fatigue, or should they engage in a short intense bout of RE to reach some threshold before fatigue sets in? Is RE contraindicated in this situation or is it possible to accumulate exercise in ten minute bouts?

Furthermore, we do not know if different outcomes can be promoted by altering the exercise prescription. Within the exercise literature it is often shown that adaptation from exercise follows the principle of specificity and various programs result in different benefits. This appears true for those with cancer, as one study showed that breast cancer survivors undergoing chemotherapy respond differently to aerobic and RE (Courneya et al., 2007). This is an important aspect to individualization as the Physical Activity and Cancer Control Framework (Courneya & Friedenreich, 2007) suggests there are six phases along the cancer continuum and in each phase exercise has a different objective. We currently do not have enough evidence to suggest what exercise regimens are the most effective at accomplishing these goals.

Recommendations for future research.

In the current review, four studies were identified that examined RE during treatment and eight were identified for RE after treatment. Many of these studies included diverse samples of cancer survivors with a variety of diagnoses and treatments making comparisons between exercise prescriptions tentative at best. As such, future research should examine the effects of RE alone with other female cancer populations, where no studies of RE are available. It is important that these studies do not combine RE with aerobics as it is difficult to isolate the effects of each exercise mode and makes it difficult to determine if the RE prescription was effective or if it offered anything beyond the aerobic activity. It will also be important to compare the efficacy of RE alone versus aerobic alone and aerobic plus RE programs in large RCTs to compare and contrast the benefits and limitations of each.

Finally, larger samples allowing for more detailed analyses will permit for the examination of any interactions between the interventions and characteristics of the survivors in the study.

While a growing body of literature has demonstrated the safety of RE and its numerous health benefits for cancer survivors, there are several gaps that still need to be addressed. Most notably, there has been a repeated call for the need to develop more tailored, cancer specific exercise prescriptions and guidelines (e.g., training frequency, intensity, and intervention timing) and to better understand how to optimize uptake and foster prolonged adherence (Buffart et al., 2014; Donnelly, Blair, Jakicic, Manore, Rankin, Smith, & ACSM, 2009; Galvao & Newton, 2005; Hayes et al., 2009; Irwin & Ainsworth, 2004; Jones, 2011; Lee et al., 2010; McNeely et al., 2006). Recognizing, time constraints as a commonly reported barrier impacting exercise adherence (Courneya et al., 2005; Rogers et al., 2007), it will be imperative to minimize time commitments by establishing a minimally effective training frequency. Although some sources suggest that once-a-week RE is a sufficient training frequency for this population (Heyward & Gibson, 2014; Lee et al., 2010), the majority of studies reviewed here have used frequencies ranging from 2-3 days per week. Of note, one study of twice-a-week RE that reported the largest strength increases in the post treatment phase with a high adherence rate (Schmitz et al., 2005).Accordingly, establishing a lowest effective training frequency is essential for maximizing adherence to effective strength training for cancer survivors. Therefore, the purpose of the present study is to directly compare once-a-week RE with twice-a-week. It is hypothesized that while both exercise programs will be efficacious, greater benefit will be derived from higher training frequency.

Chapter Three: Methods

Participants

The study protocol was reviewed and approved by the local institutional review board at CapitalHealth . Participants provided written informed consent prior to enrollment in the study and completion of any study related procedures. Eligible participants included female survivors of breast, ovarian, uterine, or cervical cancer who had: a) completed primary cancer treatment (with the exception of hormone-based therapies which may be ongoing); (b) self-reported that they have not engaged in a structured RE program within six months prior to enrollment; (c) physician approval to participate; and d) were older than 18 years of age at the time of recruitment. Participants were excluded if: a) they had participated in structured strength training within the past six months; b) had a change in medication within the past 30 days; and c) were classified as high risk based on physician responses to a health screening questionnaire that categorizes the associated risk of a survivor exercising into low, intermediate, and high categories. This health screening questionnaire is based on a review of exercise safety for cancer survivors (Jones, 2011), and excludes individuals with other chronic conditions that would be contraindications for RE (e.g., cardiovascular diseases such as previous myocardial infarction and stroke). It also excludes those with abnormal results on medical tests their physician may have ordered regardless of their relation to cancer, because they may indicate an underlying health problem. We also chose to exclude participants with osteoporosis due to concerns that predicted one repetition maximum (1RM) may pose an increased risk for bone fracture. Managed conditions not expected to significantly increase this risk such as arthritis, controlled hypertension and diabetes were

not exclusionary as such comorbidities are common among survivors (Hewitt et al., 2003; McTiernan, 2004). Survivors were asked to report any changes to these exclusion criteria during the study and were advised that any substantial changes in the medical history (e.g., cancer recurrence) or medication use (e.g., new medications) may result in their being withdrawn from the study.

Outcome Measures

Demographics and medical information.

Demographic information was gathered through self-report questionnaires and included age, sex, ethnicity, marital status, education, income, and employment status. Demographics were collected to help establish how generalizable the study is. It is a common limitation of exercise oncology studies to recruit Caucasian women with high socioeconomic status (Irwin & Ainsworth, 2004). Medical information was also collected by self-report and was also extracted from physician responses to the Physical Activity Readiness Questionnaire Medical Examination and health screening questionnaires. Medical information included information about their breast or gynecologic cancer, reoccurrences, and other cancers (e.g., time of diagnoses, stage of disease at diagnosis, and treatments received); information about comorbidities or other conditions affecting their ability to exercise; and any medications they were using at the time of the study.

Muscular strength.

Muscular strength of the upper and lower body was estimated using the Brzycki (1993) method of predicting 1RM for the bench press and leg press exercises respectively.1RM is defined as the maximum amount of weight an individual can lift for one repetition in good form and is often used as a measure of strength in exercise studies

of clinical and non-clinical populations. The protocol for estimating 1RM involved having the participant warm-up by performing 6-10 repetitions with a weight that is approximately 50% of the participant's expected 1RM. This was followed by a brief rest period up to two minutes after which the participant performed as many repetitions of the exercise as possible with a weight that should cause fatigue within 14 repetitions. If more than 14 repetitions could be performed the participant would rest again and repeat the trial using a heavier load based on the ease of the last trial. To ensure accuracy of results, no more than two additional trials were performed (Brzycki, 1993). 1RM is estimated by dividing the weight lifted by a percentage corresponding to the number of repetitions performed by the participant. Predictive tests for estimating 1RM have been previously validated in older adults ($r = 0.89$) with predictions being within 1-10kg but consistently less than the actual 1RM (Knutzen, Brilla, & Caine, 1999). Bench press 1RM has been shown to correlate with QOL in breast cancer survivors (Ohira et al., 2006).

Muscular endurance.

Muscular endurance was determined by way of a standard load test. Participants were asked to complete as many repetitions as possible on the bench press and leg press using weights corresponding to 50% of their 1RM at a cadence of 22 reps/minute. The test ended when the participant reached volitional fatigue, could no longer maintain good form, or could no longer match the set cadence. The current study's protocol was modified from other standard load tests because they use resistances that are likely to create a floor effect due to the prescribed weights likely being too great for breast cancer survivors. For example, the average bench press 1RM of breast cancer survivors in one

study was 18kg (Schmitz et al., 2005); while tests like the Young Men's Christian Association bench press test use 16kg bar (Heyward & Gibson, 2014).

The reliability of standard load tests has been previously established as excellent with repeated measures showing a high correlation (r = 0.90 - 0.98) (Cider, Carlsson, Arvidsson, Andersson, & Sunnerhagen, 2006; Invergo, Ball, & Looney, 1991). Standard load tests show convergent validity through correlations with muscular strength (P. S. Kim, Mayhew, & Peterson, 2002), while other exercises in standard protocols (heel lifts and shoulder flexion exercises) have been shown to detect expected differences between clinical and healthy populations (Cider et al., 2006).

Body composition.

Body composition was assessed using whole body bioelectric impedance (*Tanitia Body Composition Analyzer, Model TBF-215*). This method was chosen because of its non-invasive nature which makes it more acceptable to survivors than methods such as measuring skinfolds or underwater weighing, and because of the greater costs associated with measures such as duel energy X-ray absorptiometry and magnetic resonance imaging. Measurements of body composition included LBM, %BF, total body fat, and weight. As the accuracy of bioelectrical impedance is susceptible to changes in hydration status such as exercise, eating/drinking, alcohol and diuretic use immediately before testing was discouraged (Heyward & Gibson, 2014; Kushner, Gudivaka, & Schoeller, 1996). Specifically, participants were required to not exercise 12 hours prior to testing and to also not eat or drink four hours prior. Participants using diuretics to control blood pressure were asked before testing if these drugs have been taken at their normal time.

According to Heyward, if these conditions are met bioelectric impedance has a standard error of measurement between 2.7-4.0%.

Quality of life.

QOL was assessed using the MOS-SF36 (Ware & Sherbourne, 1992). The MOS-SF36 is a self-administered measure of QOL with eight subscales including: physical function, role-physical, bodily-pain, general health, vitality, social functioning, role-emotional, and mental health. The measure has been previously validated (Davies, Gibbons, Mackintosh, & Fitzpatrick, 2009) and has been shown to have superior sensitivity to changes in QOL compared to the FACT measurement system in at least two RCTs of exercise in a cancer population (Cadmus et al., 2009; R. Segal et al., 2001).

Fatigue.

Fatigue was measured using the fatigue subscale of the FACT measurement system (Yellen et al., 1997). The FACT-F is a 13 item questionnaire that measures the degree to which a cancer survivor experiences fatigue. The FACT-F has also been widely used to determine the effectiveness of interventions aimed toward reducing fatigue (Stone & Minton, 2008). The instrument has also been shown to be a reliable and valid measure of fatigue (Yellen et al., 1997).

Physical activity.

Moderate to Vigorous Physical Activity (MVPA) was monitored using the Godin Leisure-Time Exercise Questionnaire (GLTEQ) (Godin & Shephard, 1985). This self-report questionnaire has been shown to have good to excellent test-retest reliability for both moderate (r = 0.36-0.46) and strenuous (r = 0.84-0.94) physical activity (Sallis, Buono, Roby, Micale, & Nelson, 1993). Validation studies have shown that the GLTEQ

is related to VO_2max (r = 0.38), body fat percent (r = -0.42), accelerometry (= 0.32-0.45), and other physical activity questionnaires (r = 0.54-0.61) (Jacobs, Ainsworth, Hartman, & Leon, 1993; Miller, Freedson, & Kline, 1994). MVPA was calculated by adding total time of moderate and vigorous physical activity together. Participants who meet 150 minutes of moderate to vigorous physical activity are considered to be meeting physical activity guidelines for the general population (Donnelly et al., 2009).

Process Measures

Process measures were included to provide valuable information about participant recruitment, program adherence (i.e., percentage of assigned sessions completed) and compliance (i.e., the degree to which participants were able to follow the program they were given, expressed as a percent of the total number of sets prescribed), and safety. In regard to safety, participants were instructed to report any adverse event that occurred during their participation in the study regardless of its expected cause.

Experimental Design and Procedures

The present study used a randomized quasi-experimental design with two groups serving as their own controls. Potential participants contacted the lead investigator (Mr. Gravelle) by responding to print advertisements posted in oncology wards, physicians' offices, and cancer support groups. Information packages were then mailed to those who expressed an interest by contacting the lead investigator. Packages included a consent form describing the study, a baseline questionnaire, and health screening questionnaires.

Eligible, consenting participants began the 13 week program by first completing a one-week resistance training familiarization program. The familiarization week consisted of one set of 10-14 repetitions using universal machines (leg press, chest press, seated

row, leg extensions, shoulder press, leg curls, latissimus pull-down) and two core stability exercises done to fatigue (front plank, and side plank). Participants were asked to choose weights that would allow them to complete the prescribed number or repetitions without going to failure (approximately 50-60%1RM). This familiarization was not expected to cause changes in this study's outcomes because of its use of low training volume, resistance, and duration. Baseline assessments were completed at the end of this week. Follow-up fitness assessments were conducted at mid-program (at the end of 7th week of their participation), and again at the conclusion of the study (at the end of their 13th week of participation. All tests were conducted in the morning by Mr. Gravelle.

Following the baseline fitness assessments participants were randomized into either the once-a-week or twice-a-week RE groups and began a 12 RE program. Randomization was done using a randomized balanced control technique to stratify the groups on tamoxifen use, physical activity levels (meeting guidelines to accumulate 150 minutes of moderate-vigorous physical activity), and clinical levels of fatigue according to Cella and colleagues (2002) (FACT-F scores $\geq$ 36). Stratifying the groups by hormone use was congruent with recommendations made by Irwin & Ainsworth (2004). Additionally, hormone therapies such as tamoxifen can decrease insulin-like growth factor I as much as 16% (Bonanni et al., 2001) and could potentially hinder strength development (Kraemer & Ratamess, 2005). Stratifying groups on physical activity levels was also necessary because physical activity levels have been shown to be related to QOL and fatigue in cancer survivors (McNeely et al., 2006). Lastly, as exercise has a limited ability to reduce fatigue in asymptomatic survivors, groups were balanced on this characteristic as well. The clinical significance of the FACT-F tool (scores $\geq$ 36) has been

established and is based on the cut-offs association with hemoglobin levels, patient fatigue ratings, and positive responses to chemotherapy (Cella et al., 2002).

Description of the Interventions

Survivors met once or twice a week, depending on group assignment, at a scheduled time for supervised, group-based RE. If participants missed a session they were unable to make up the lost session. All training sessions (including those in the familiarization program in the first week) were supervised by a Canadian Society for Exercise Physiology – Certified Exercise Physiologist (Mr. Gravelle) and lead with the assistance of female undergraduate kinesiology volunteers. Both the once-a-week and twice-a-week groups followed the same RE program with the only difference between groups being the number of sessions each week. This program used the same exercises as the familiarization program, but at a higher intensity and volume. Exercises were done for two sets of 10-14RM (approximating 65-75%1RM) for the first six weeks. For example, with a given weight a survivor may be able to perform 11 repetitions before reaching volitional fatigue, as this exercise becomes easier they may be able to perform more repetitions, once 14 repetitions can be performed on all sets the weight was increased as long as a minimum of 10 repetitions could be performed with the new weight. After six weeks participants progressed by performing an additional set of the same exercises and continued to exercise for an additional six weeks (sets continued at 10-14 repetitions at 65-75%1RM). Resistance was increased only when the participant was able to perform more than 14 repetitions for each set. Weight was not increased by more than 10lbs for lower body exercises and 5lbs for upper body exercises at any one time. Sessions of RE began and ended with a ten minute aerobic warm-up and cool down.

Primary Data Analysis

Statistical analysis was performed using *International Business Machines* Statistical Package for Social Sciences v. 20. The data were examined for normality using histograms and calculations of skewness and kurtosis to meet the assumptions of parametric tests. Missing data were handled using the last observation carried forward method in order to preserve power. Descriptive measures of central tendency have been presented as means and standard deviations. An alpha level of 0.05 was used for all statistical tests. Regardless of statistical significance, effect sizes and observed power have also been reported due to the exploratory nature of this study. Effect sizes (partial eta squared; η^2), are defined according to Cohen's guidelines [small (0.02); medium (0.13); large (0.26); (Cohen, 2013)]. For observed power, values $\geq$0.8 indicate a lower chance of committing a type II error.

Baseline comparisons of demographics, cancer history, and study outcomes were made by using an independent samples t-test for continuous data and chi square analysis for categorical data. To analyze the impact of once-a-week versus twice-a-week strength training study outcomes were analyzed using a factorial repeated measure analysis of variance (ANOVA). Comparisons were made using Wilks' Lambda distribution when assumptions of equal variance were satisfied. When these assumptions were violated Pillai's trace was used. Bonferroni pairwise comparisons were used on significant findings to establish when significance occurred during the course of the study.

Chapter Four: Results

Participants

Study participants were recruited between November 2012 and March 2014. During this time a total of 34 breast and ovarian cancer survivors contacted the research team with an interest in learning more about the study. Intake packages, which included consent forms, activity suitability and risk assessments, and baseline questionnaires, were forwarded to survivors by mail (Figure 1). Fifteen of the 34 packages (44%) were returned with signed consent forms. Of these, one participant withdrew prior to their baseline fitness assessment because they were concerned that the weight training program might aggravate their elbow tendinitis. Upon baseline screening, it was also noted that three breast cancer survivors indicated that they had a diagnosis of osteoporosis and were consequently deemed ineligible and were excluded from the study. The remaining 11 consenting survivors were randomized to either the 1 day/week (n=5) or 2 day/week (n=6) strength training conditions. Two participants withdrew before their midpoint assessments. One withdrew because they returned to work and one due to pneumonia.

Baseline demographic and medical characteristics of those randomized are presented in Table 7. No statistical differences between groups were found at baseline, although differences in bodily pain approached significance ($t(9) = 2.23$, $p = 0.05$), with the twice-a-week group reporting greater pain (1 day/week $M = 80.6$, $SD = 14.4$; 2 days/week $M = 55.5$, $SD = 21.3$). No significant changes in total physical activity levels (moderate-to-vigorous minutes/week) were noted between groups ($F(1, 10) = 0.83$, $p = 0.39$) or over the course of the intervention (Wilks' Lambda = 0.558 $F(1, 9) = 3.17$, $p = 0.10$).

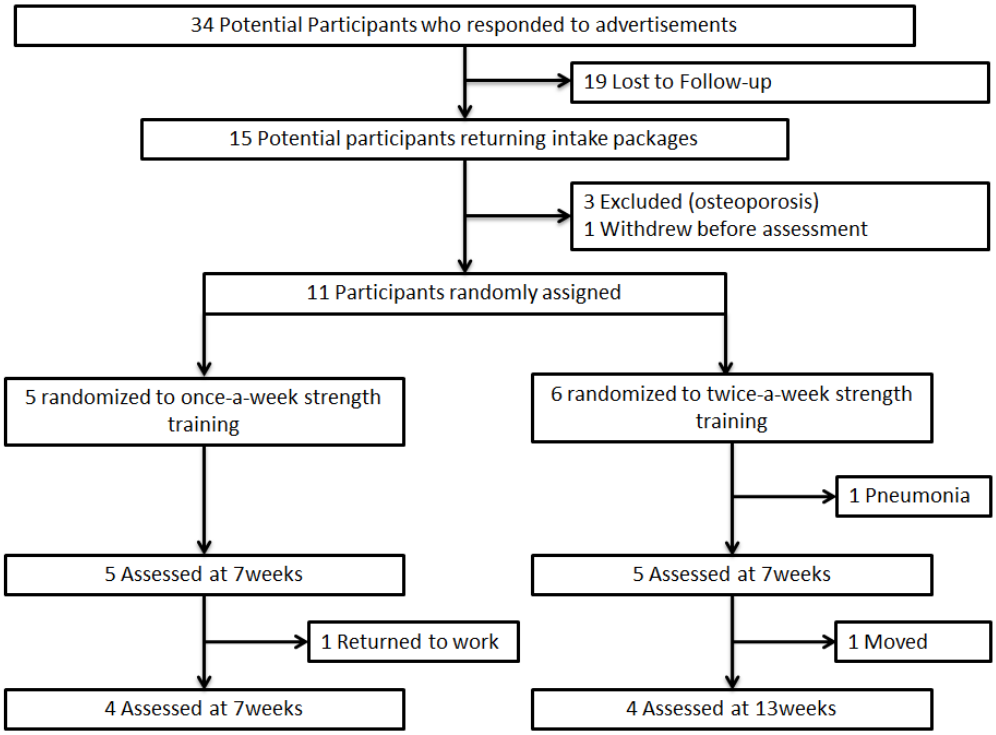

Figure 1. Participant flow through the study.

Outcome Measures

Muscular fitness.

After 13 weeks of strength training, a significant main effect for time on all measures of muscular strength was found (Table 8). No significant interactions or main effects comparing the two exercise groups were found. 1RM leg press increased on average of 14.3% (*SD* = 15.1%) in the 1 day/week group, while the 2 days/week group increased an average of 23.4% (*SD* = 11.7%) (Figure 2). For the bench press, average 1RMs increased 8.5% (*SD* = 15.7%) and 28.6% (*SD* = 28.7) for the 1 day/week and 2 days/week groups respectively (Figure 2). These results remained unchanged when examining strength gains relative to the participant's body weight (Figure 2). For muscular endurance, the once-a-week group showed an average increase in repetitions to

Table 7. Baseline participant characteristics.

Measure	Overall (n = 11)	1 day/week (n = 5)	2 days/week (n = 6)	*p*
Demographics				
Married	8			
Completed University or College	8			
Income > $50,000	4			
Full Time Employment	5			
Age	53.5(8.1)	53.4(8.1)	53.5(8.9)	0.92
MVPA (min/week)	121.8(201.2)	64.0(89.6)	170(261.6)	0.41
Cancer History				
Breast	8	3	4	0.82
Ovarian	4	2	2	
Years Since Diagnosis	8.1(5.5)	6.8(10.8)	9.2(7.1)	0.67
Years Since Last Treatment	5.5(8.4)	5.2(11.1)	5.8(6.0)	0.92
Chemotherapy or radiation	5			
Chemotherapy and radiation	5			
Muscular Fitness				
Leg Press 1RM (kg)	123.4(33.3)	117.3(37.3)	128.56(32.2)	0.60
Bench Press 1RM (kg)	25.8(6.6)	23.7(3.2)	27.5(8.4)	0.37
Leg Press Standard Load Reps	35.3(8.3)	34.6(7.1)	35.8(9.8)	0.82
Bench Press Standard Load Reps	27.5(9.7)	28.6(9.9)	26.5(10.3)	0.74
Body Composition				
Body Mass Index (kg/m^2)	26.1(5.6)	26.2(6.1)	26.0(5.7)	0.97
Fat Free Mass (kg)	44.8(3.9)	43.4(4.6)	45.9(3.2)	0.19
Percent Body fat (%)	35.5(7.5)	33.5(9.3)	37.2(5.9)	0.49
Quality of Life				
Physical Functioning	72.5(29.9)	76.4(39.65)	69.2(22.5)	0.32
Role Physical	62.5(37.3)	65(39.2)	60.4(39.3)	0.85
†Bodily Pain	66.9(21.9)	80.6(14.4)	55.5(21.3)	0.05
General Health	52.2(30.3)	61.2(26.9)	44.7(33.2)	0.40
Vitality	52.8(30.4)	57.5(31.4)	49.0(32.0)	0.67
Social Functioning	65.9(32.6)	72.5(28.5)	60.4(37.4)	0.57
Role Emotional	68.9(38.2)	68.3(39.3)	69.4(41.1)	0.96
Mental Health	56.4(33.9)	51.0(36.3)	60.8(34.6)	0.66
Physical Component Score	46.9(9.70	52.2(10.8)	42.5(6.6)	0.10
Mental Component Score	41.4(20.9)	40.8(21.1)	41.9(22.7)	0.94
Fatigue	35(15.8)	40.6(15.1)	30.6(16.3)	0.32

Note: * Higher scores indicate better quality of life and less pain and fatigue. See Appendix L for additional analysis of MVPA. Cell sizes smaller than 5 have been removed to protect participant confidentiality. MVPA = moderate to vigorous Physical activity.
† p =0.053.

fatigue on the leg press standard load test by 57.0% (*SD* = 72.0%) and 41.1% (*SD* = 18.7%) for the bench press test. The average improvement of the twice-a-week group was comparable for both the leg press (*M* = 58.0%, *SD* = 56.6%) and bench press tests (*M* = 46.4%, *SD* = 42.2%). Bonferroni pairwise comparisons revealed that by the 7th week of the study only the bench press standard load test showed significant improvement ($p < 0.01$), while the leg press standard load test and 1RM tests required the full 13 weeks to reach significance ($p < 0.05$).

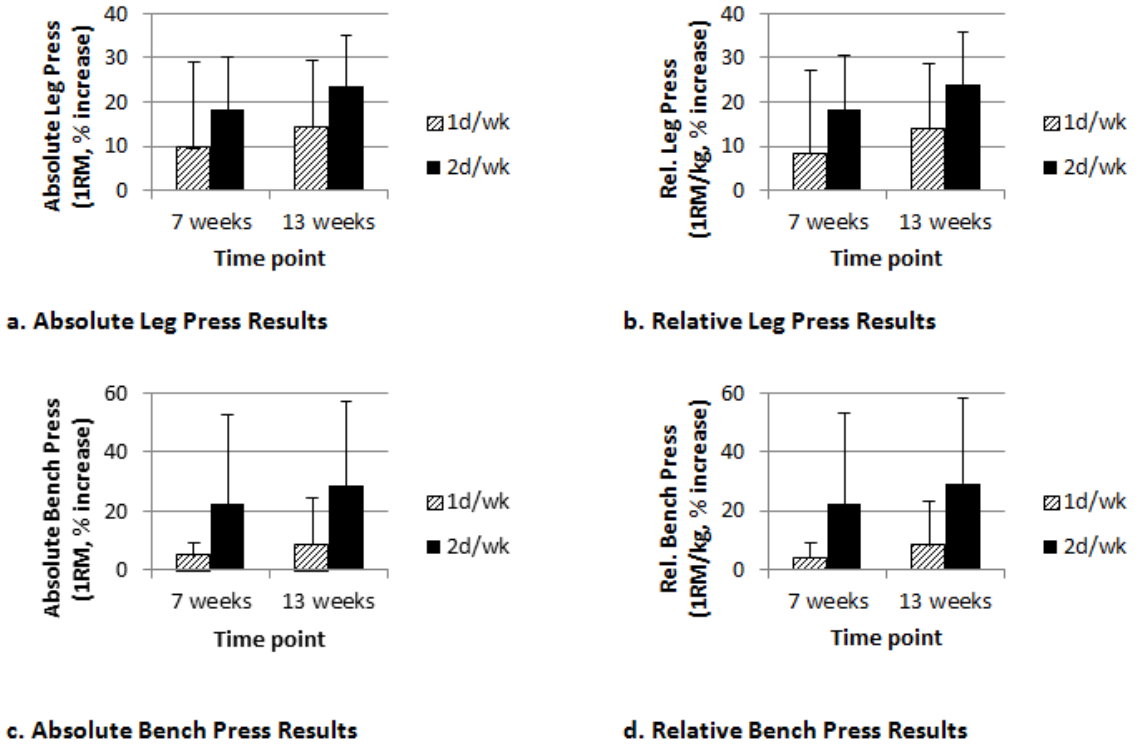

Figure 2. Absolute and relative changes in 1RM by group. Within group increases are significant for both groups at 13 weeks ($p \leq 0.05$), between group differences are insignificant.

Table 8. Changes in muscular fitness outcomes.

Measure	Group	Baseline	Week 7	Week 13	Repeated Measures ANOVA			
		M (SD)	M (SD)	M (SD)	Analysis	η2	Power	*p*
Leg Press	1d/wk	117.3(37.2)	123.2(16.9)	132.0(36.4)	Within	0.72	0.92	0.01**
1RM (kg)	2d/wk	128.6(32.2)	153.0(46.1)	159.1(46.3)	Between	0.11	0.16	0.324
Bench Press	1d/wk	23.7(3.2)	25.0(4.0)	25.9(5.9)	Within	0.57	0.67	0.03*
1RM (kg)	2d/wk	27.5(8.4)	31.6(5.0)	33.6(6.4)	Between	0.27	0.36	0.11
Leg Press	1d/wk	34.6(7.1)	44.4(18.4)	53.0(24.0)	Within	0.52	0.57	0.05
SLT (reps)[a]	2d/wk	35.9(9.8)	45.3(4.0)	52.7(17.1)	Between	0.00	0.05	0.93
Bench Press	1d/wk	28.6(9.9)	37.4(11.8)	39.0(9.7)	Within	0.87	1	0.00***
SLT (reps)	2d/wk	26.5(10.3)	33.8(8.7)	36.7(11.6)	Between	0.02	0.07	0.67

Note: η2 = Partial eta Squared. 1RM = One repetition maximum. SLT = Standard load test. 1d/wk = Once-a-week group. 2d/wk = Twice-a-week group.
[a] Pillai's trace.
*p< 0.05. **p<0.01. ***p<0.001

Table 9. Changes in body composition outcomes.

Measure	Group	Baseline	Week 7	Week 13	Repeated Measures ANOVA			
		M (SD)	M (SD)	M (SD)	Analysis	η2	Power	*p*
Weight	1d/wk	69.3(14.7)	69.9(13.8)	69.4(13.8)	Within	0.39	0.37	0.14
(kg)	2d/wk	73.8(11.1)	73.8(11.1)	73.5(11.1)	Between	0.03	0.08	0.60
Lean Body	1d/wk	43.4(4.6)	43.4(4.3)	43.0(4.5)	Within	0.09	0.09	0.70
Mass (kg)[a]	2d/wk	45.9(3.2)	42.6(8.9)	46.0(3.7)	Between	0.04	0.08	0.57
Body Fat	1d/wk	33.5(9.3)	36.7(8.4)	36.8(8.5)	Within	0.21	0.17	0.39
(%)	2d/wk	37.2(5.9)	36.9(6.0)	36.8(5.7)	Between	0.01	0.06	0.78

Note: η2 = Partial eta Squared. 1d/wk = Once-a-week group. 2d/wk = Twice-a-week group.
[a] Pillai's trace.

Body composition.

No changes in body composition were observed in this study (Table 9).

Quality of life and fatigue.

After 13 weeks of strength training, there were no significant changes in any of the QOL sub-scales or measures of fatigue (Table 10).

Process Measures

Intervention compliance was high for both groups (1 day/week: $M = 94.7\%$, $SD = 2.8$; 2 day/week: $M = 97.7\%$, $SD = 4.1$). However, it was noted, there was a considerable difference between the study groups on adherence (1 day/week: $M = 83.3\%$, $SD = 19.6$; 2 day/week: M 65.2%, $SD = 21.7$) $t(9) = 1.44$, $p = 0.18$). Although this difference was not statistically significant it may still be meaningful in the interpretation of the study's results where the effect of training frequency was the primary concern. Consequently, to help discern the true effect frequency of RE had in the study an additional ANOVA was performed comparing participants who, on average, attended less than 1 day/week (low actual frequency – low) with those who attended one or more days/week (high actual frequency – high). Splitting the data at this point appears to be the best method of handling the data because the resulting groups are approximately equal (Low n = 5, High n = 6), and it mainly preserves the purpose of the study which was to compare once-a-week and twice-a-week strength training.

The average number of sessions attended by the high actual frequency group was 16.8±3.9 days; the average for the low actual frequency group was 9.4±2.1 ($p = 0.04$). Additional correlations between the number of sessions attended and study outcomes were also made to help further quantify the relationship between strength training

Table 10. Changes in quality of life and fatigue outcomes.

Measure	Group	Baseline	Week 7	Week 13	Repeated Measures ANOVA			
		M (SD)	M (SD)	M (SD)	Analysis	η2	Power	*p*
Physical Funct.	1d/wk	76.4(39.7)	74.4(39.7)	74.4(39.7)	Within	0.35	0.32	0.16
	2d/wk	69.2(22.5)	81.7(12.9)	80.0(12.2)	Between	0.00	0.05	0.92
Role Physical	1d/wk	65.0(39.2)	76.3(39.4)	63.8(44.7)	Within	0.24	0.2	0.33
	2d/wk	60.4(39.3)	67.7(35.0)	64.6(38.5)	Between	0.00	0.05	0.86
Bodily Pain[a]	1d/wk	80.6(14.4)	68.8(10.0)	77.4(22.2)	Within	0.22	0.19	0.36
	2d/wk	55.5(21.3)	55.7(27.0)	59.2(26.8)	Between	0.21	0.28	0.16
General Health	1d/wk	61.2(26.9)	69.6(24.3)	63.8(29.8)	Within	0.20	0.17	0.40
	2d/wk	44.7(33.2)	50.5(42.6)	45.5(33.4)	Between	0.09	0.13	0.37
Vitality	1d/wk	57.5(31.4)	60.0(27.5)	52.5(30.2)	Within	0.10	0.10	0.66
	2d/wk	49.0(32.0)	53.1(30.8)	50.0(31.9)	Between	0.01	0.06	0.75
Social Funct.	1d/wk	72.5(28.5)	80.0(32.6)	75.0(35.4)	Within	0.39	0.37	0.14
	2d/wk	60.4(37.4)	79.2(40.1)	62.5(44.0)	Between	0.02	0.07	0.70
Role Emotion	1d/wk	68.3(39.3)	81.7(41.0)	76.7(39.7)	Within	0.28	0.24	0.26
	2d/wk	69.4(41.1)	73.6(38.9)	73.6(38.9)	Between	0.00	0.05	0.89
Mental Health	1d/wk	51.0(36.3)	67.0(29.3)	68.0(32.5)	Within	0.23	0.19	0.35
	2d/wk	60.8(34.6)	66.7(34.0)	62.5(33.6)	Between	0.00	0.05	0.95
PCS	1d/wk	52.2(10.8)	50.9(5.0)	49.8(13.1)	Within	0.02	0.06	0.92
	2d/wk	42.5(6.6)	45.3(8.6)	45.0(8.5)	Between	0.16	0.21	0.23
MCS	1d/wk	40.8(21.1)	46.4(20.3)	44.5(20.3)	Within	0.22	0.18	0.37
	2d/wk	41.9(22.7)	45.4(22.3)	42.1(22.2)	Between	0.00	0.05	0.95
Fatigue	1d/wk	40.6(15.1)	32.6(13.2)	36.8(15.8)	Within	0.10	0.10	0.64
	2d/wk	30.6(16.3)	34.5(16.1)	32.7(18.3)	Between	0.02	0.07	0.68

Note: Higher scores represent better quality of life and lower fatigue. η2 = Partial eta Squared. Funct. = Functioning; PCS = Physical Composite Score. MCS = Mental Composite Score. 1d/wk = Once-a-week group. 2d/wk = Twice-a-week group.

[a] Pillai's trace.

frequency and its benefits. The most common reasons given by participants for missing sessions were planned vacations, health problems (such as the flu or medical appointments) and scheduling conflicts.

Muscular fitness.

Subsequent analysis using the low and high actual frequency splits revealed several group×time interactions that were not observed when comparing original groups. For the muscular fitness tests, the group×time interaction for the 1RM leg press became significant (Wilks' Lambda=0.182, $F(2,8)$ 17.95, $p < 0.01$) (Figure 3). The high actual frequency group increased leg press 1RMs on average 30.5% (SD = 4.8); in contrast the low actual frequency group increased 6.0% (SD = 4.5). The 1RM bench press interaction approached significance (Wilks' Lambda = 0.491, $F(2,8)$ 4.15, $p = 0.06$) (Figure 4). The high actual frequency group increased bench press 1RM on average 33.1% (SD = 25.7); while the low actual frequency group increased 3.4% (SD = 12.53). Correlational analysis showed that the number of completed sessions was related to the percent increase in 1RM leg press after 13 weeks ($r = 0.64$, $p = 0.03$) (Figure 5). This relationship was not found to be significant for bench press 1RMs ($r = 0.26$, $p = 0.44$). Dividing the groups based on these splits did not influence the muscular endurance results.

Quality of life.

Group×time interactions for physical functioning (Wilks' Lambda = 0.504, $F(2,8)$ 3.93, $p = 0.07$), and fatigue (Wilks' Lambda = 0.501, $F(2,8)$ 3.99, $p = 0.06$) approached significance. For physical functioning there was a slight decrease observed in the low actual frequency group (*pre* M = 73.4, SD = 38.4; *post* M = 71.4, SD = 38.3), while the

high actual frequency group improved (*pre M* = 71.67, *SD* = 24.63; *post M* = 82.5, *SD* = 13.7) $p = 0.07$. For fatigue, the low actual frequency group experienced a slight worsening in symptoms (*pre M* = 33.2, *SD* = 19.6; *post M* = 29.4, *SD* = 18.3) while those with high actual frequency showed improvement (*pre M* = 36.8, *SD* = 13.7; *post M* = 38.8, *SD* = 15.0) $p = 0.06$. Direct correlations between the number of sessions attended and changes in physical functioning ($r = 0.44$, $p = 0.17$) and fatigue ($r = 0.26$, $p = 0.45$) were insignificant. Examining the data using actual training frequency did not alter any of the body composition outcomes.

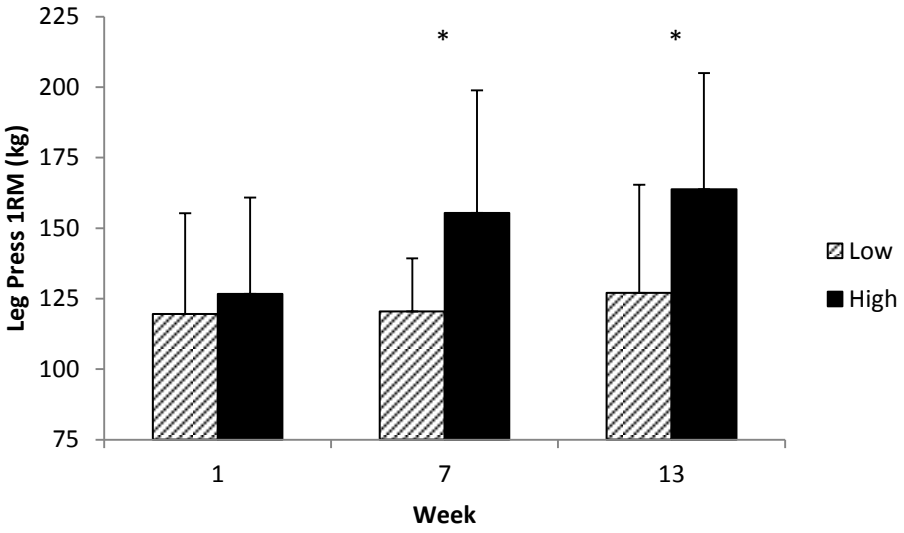

Figure 3. Predicted leg press 1RMs for participants attending less than 1 day/week (Low) and one or more days/week (High). Group×time interaction is significant ($p < 0.05$).
*Significant differences between means

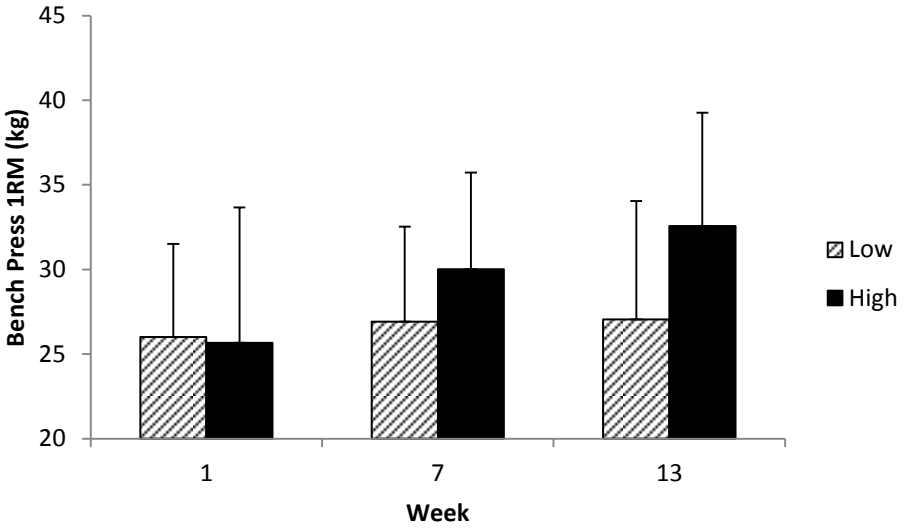

Figure 4. Predicted bench press 1RMs for participants attending less than one day/week (Low) and one or more days/week (High). Group×time interaction approaches significance ($p = 0.06$).

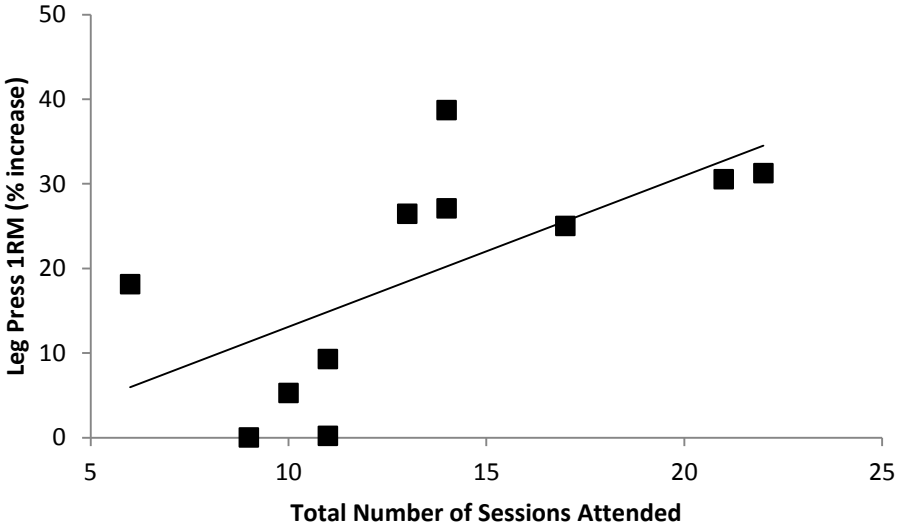

Figure 5. Correlation between number of sessions attended over the course of the study and percent increase in predicted leg press 1RMs after 13 weeks ($r = 0.64$, $p = 0.03$).

Adverse Events

No serious AEs occurred as a result of RE in the present study. However, all survivors reported some delayed onset muscle soreness during the study, usually after initiating the program or following a fitness assessment. Eight minor events did occur which may have be attributed to RE program. These included four new musculoskeletal injuries affecting the knees (2), wrists (1), and hands (1); two previous musculoskeletal injuries (1 back, 1 knee) that were aggravated by strength training; one case of syncope (participant hyperventilated during a front plank), and one case of skin irritation on the forearms following the front plank. One participant was prevented from increasing the weight on the leg extension exercise until their knee injury was resolved. No other modifications to the exercise program or activities of daily living were reported. No AEs required hospitalization; however one survivor developed pneumonia and had to withdraw from the study.

Chapter Five: Discussion

The purpose of this study was to examine the impact of once versus twice-a-week RE in breast and gynecologic cancer survivors. Overall, the results of the present study demonstrate that RE, regardless of training frequency, leads to increased muscular strength and endurance in survivors of both breast and ovarian cancer. Additional comparisons made between survivors who were able to attend one or more sessions per week versus those who were not provide preliminary evidence suggesting that training frequency plays an important role in the dose response for this population.

Muscular Fitness

The main finding of the present study was the increase in strength observed in both groups of participants. After 13 weeks, leg press 1RMs increased 14% in the once-a-week group and 23% in the twice a week group. Bench press 1RMs increased 9% and 29% for the once-a-week and twice-a-week groups respectively. In relation to other strength training studies of breast cancer survivors, improvements in leg press 1RM ranged between 19.9% to 39% and bench press 1RM ranged from 12.4% to 63% for those randomized to a strength training program (Musanti, 2012; Ohira et al., 2006; Rajotte et al., 2012; Schmitz et al., 2009; Schmitz et al., 2005; Winters-Stone et al., 2012). Interestingly, control groups in these studies also demonstrated strength improvements, possibly due to survivors simply recovering from cancer treatment. In these studies, controls typically increased leg press 1RMs between 7.1% to 9.8% and bench press 1RMs between 2.3% to 12%. Based on the comparison with control groups in previous studies (Musanti, 2012; Ohira et al., 2006; Rajotte et al., 2012; Schmitz et al., 2009; Schmitz et al., 2005; Winters-Stone et al., 2012), strength training once-a-week does not appear to be an effective training frequency.

Additional comparisons in strength gains made between those survivors who trained less than once-a-week to those who trained more, further support the need to encourage strength training more than once-a-week. Specifically, those survivors who attended more than one-session per week increased leg strength by 31% and upper body strength by 33%, while those attending less frequently saw minimal improvements in leg press (6%) and bench press (3%) strength. While the present study failed to detect any statistical difference between the randomly assigned training groups, comparisons with other literature, coupled with the results of comparing training frequency independent of group assignment, suggests that strength gains made from once-a-week training, while statistically significant, are minimal.

The strength gains in the present study fell somewhat short of expectations. The most effective exercise prescription in the cancer literature was done by Schmitz and colleagues (2005) and increased leg press 1RM 39% and bench press 1RM 63%. This study, used a very traditional RE prescription of twice weekly RE done for three sets of 10-12RM. The use of this type of prescription is well supported by exercise prescription literature. For example, the meta-analysis by Rhea and colleagues (2003) supports this training intensity for untrained individuals, stating that for healthy individuals with less than one year of training experience, maximal strength gains are realized with a 12RM training intensity. The use of multiple sets and twice weekly training frequency was also supported by this meta-analysis, although four sets was deemed optimal. Galvao & Newton (2005), suggest that exercise prescription for cancer survivors should be guided by the wealth of information available discussing improving fitness in the general population. This notion is supported for breast cancer survivors based on how similar the optimal prescription for untrained individuals recommended by Rhea et al. (2005) is to the program offered by Schmitz (2005).

To our knowledge, this is the first strength training study to use muscular endurance as an outcome following treatment. Unlike our 1RM findings, improvements in muscular endurance did not seem to differ between groups nor those with high and low actual frequency (~57%). These increases in lower body endurance (~57%) and upper body endurance (~43%) were the largest observed in the present study. This is likely because the 10-14RM training intensity is more associated with increases in muscular endurance rather than strength, especially when compared to other training ranges with heavier weights designed to increase strength and promote hypertrophy (Anderson & Kearney, 1982; Campos et al., 2002). In determining what constitutes an optimal training frequency for cancer survivors, it is important to consider that all aspects of muscular fitness (strength, power, endurance, and hypertrophy) should be promoted as they likely translate to unique aspects of QOL, such as the ability to perform a variety of activities of daily living (e.g. carrying groceries, opening heavy doors, getting out of chairs) and healthier body image. Studies examining activities of daily living in cancer survivors would be useful for determining which aspects of strength are most important for survivors.

For survivors, especially older survivors, it is important to keep in mind that benefit from RE does not necessarily have to be associated with increases in muscular fitness. Preserving muscle function is important if increases in fitness are not possible. As people age, regardless of cancer history, the expected trend is for a decrease in muscle mass and strength (Kallman, Plato, & Tobin, 1990). Since physical inactivity is partially responsible for this aging problem (Kallman et al., 1990), it may be exacerbated in cancer survivors who typically are not as physically active as their healthy counterparts (Blanchard et al., 2008). Based on this perspective, and data collected in this study, there is still value in once-a-week RE.

Quality of Life and Fatigue

In contrast to similar post treatment studies (Kim et al., 2010; McKenzie & Kalda, 2003; Rajotte et al., 2012; Schmitz et al., 2005) the present study failed to show that RE, either once-a-week or twice-a-week, improved QOL or fatigue. This is likely due to a lack of statistical power, although it is also possible that because baseline fatigue was just below that of clinical fatigue there was not much room for improvement (Baseline Fatigue *M* 35, *SD* = 15.8). At baseline, only the twice-a-week group had FACT-F scores low enough to be considered clinically fatigued (*M* = 30.6, *SD* = 16.3); this did not change by the conclusion of the study (*M* = 32.7, *SD* = 18.3) ($\eta^2 = 0.10$). Although not statistically significant, it is worth noting the large effect sizes that were also observed for within group comparisons of social functioning ($\eta^2 = 0.39$), physical functioning ($\eta^2 = 0.35$), and emotional role functioning ($\eta^2 = 0.39$). Observed power for these three outcomes ranged from 0.24-0.37 further supporting that the sample size was inadequate.

The null findings in QOL are interesting since the present study did observe substantial increases in muscular fitness which is thought to mediate improvements in QOL (Ohira et al., 2006). Of the different aspects of QOL, physical functioning has been shown to improve more consistently than other aspects of QOL as a result of participating in an exercise program because increases in fitness directly transfer to daily living tasks such as lifting or carrying groceries. However, in the present study, many survivors appeared to already have sufficient levels of fitness to carry out these activities. For example, physical functioning was rated higher than any other facet of QOL at baseline. Additionally, the average physical activity level of the participants was just 30 minutes below guidelines promoting 150 minutes of moderate to vigorous intensity minutes per week; and had lower body strength exceeding their body weight (meaning they would easily be able to stand up from a squatted position). Together, this suggests

that perceived physical functioning may not have been enhanced by the increases in strength and muscular endurance seen in this study because most survivors had already reached a threshold needed to perform daily tasks. Future studies should strive to recruit more sedentary participants or those participants who are closer in time to the completion of cancer treatment.

An alternate explanation for the null findings in QOL may be due to the low adherence rate of the twice-a-week group. Group×time interactions using the actual training frequency splits showed that low frequency was associated with decreases in physical functioning and worsening fatigue, while high frequency lead to better physical functioning and improvements in fatigue. As mentioned, those in the low actual frequency group did not increase muscular fitness, the mechanism by which RE improved QOL and fatigue (Ohira et al., 2006). Together, these findings further support the position that improvements in QOL resulting from exercise are mediated by increases in physical fitness.

While group dynamics were not targeted within the current study, the large effect sizes observed for social functioning and role emotional may be attributed to the informal group exercise setting. Specifically, exercising with a group allows survivors to socialize with others going through similar circumstances. This socialization may also involve sharing emotional problems which may be met with empathy and solutions to emotional problems may be given. For example, Adamsen and colleagues (2001) described a kind of collective reciprocity which occurred in a group of male cancer survivors. In this study, participants formed new friendships and the social benefits were described as "markedly positive" (p. 533). The authors felt that this was possible because of the commonality of being a cancer survivor made members of the exercise group feel like normal members of a group rather than abnormal because of their health. Emilie and colleagues (2007) reported similar trends with a group of breast cancer survivors. In

discussion groups, these survivors felt that the empathy they received from one another helped them feel less isolated. They also formed friendships and shared information related to their disease such as obtaining government benefits as a survivor.

In the present study, it was noticed that survivors would not only support each other with empathy, friendship, and information but also in tangible ways such as ride sharing or inviting others to join other opportunities for physical activity at the conclusion of the study. Survivors also benefited from the group setting through modeling; observing other survivors who were successful in the study. This was encouraging for new survivors who initially found the RE intervention difficult because it allowed them to see another woman with a similar circumstance (i.e. surviving cancer) and believe they too could be successful. According to (Duncan & McAuley, 1993), social support, such as this, positively impacts adherence to exercise by way of bolstering self-efficacy. In this way, the group based format was a benefit to the study. However, the low adherence rate suggests the full benefits of group based exercise were not fully realized. Incorporating more specific group based activities, such as exercises that require partnership to complete (e.g. towel pulling standing crunch/bicep curls), may be one way to maximize the benefits of group exercise.

Body Composition

The present study was unable to detect significant changes in its body composition measures, despite expectations that LBM would increase. A large but insignificant effect was found for changes in weight, but this appears misleading since body weight did not change more than 0.6kg at any point in the study. The reason for the null finding is most likely due to sample size limitations, however other explanations cannot be ruled out.

Most other studies of post treatment cancer survivors show that LBM improves following strength training (LaStayo et al., 2011; Schmitz et al., 2005; Winters-Stone et al., 2011). These studies all assessed body composition using more sophisticated technology than the bioelectric impedance analyzer used in the present study, specifically duel energy X-ray absorptiometry (Schmitz et al., 2005; Winters-Stone et al., 2011) and cross sectional area via magnetic resonance imaging (LaStayo et al., 2011). Additionally, the protocols of Schmitz and Winters-Stone used a yearlong strength training intervention allowing considerable time for changes to occur.

It has been recommended that exercise interventions for survivors should use protocols of at least 12 weeks in duration to allow physiologic adaptations to take place (Irwin & Ainsworth, 2004). However, data from the present study and also from Rajotte et al. (2012) suggests this may not be sufficient if body composition is a primary endpoint of strength training. To date, the only study to show an increase in LBM in 12 weeks or less was by LaStayo and colleagues (2007), and no study has shown fat mass or body fat percentage to decrease in this short time period. This is because early increases in strength are primarily due to neural adaptations and hypertrophy of muscle cells does not begin until 6-7 weeks (Phillips, 2000). Since cancer is typically a disease that occurs later in life most survivors are older and may be somewhat resistant to muscle hypertrophy, this seems especially true for women (Charette et al., 1991). Given this, more than 12 weeks should be allotted to training programs to allow lean body mass to increase. However, the average age of participants in the current study was 53.5±8.1, suggesting other factors, such as adherence, may have also limited increases in LBM. A second consideration is that strength training is not as efficient as aerobic modalities combined with nutritional interventions at reducing body fat. Studies using body composition as an endpoint

should consider not only their methods for assessing body composition, but also the duration of their interventions which should include aerobics and diet.

Adverse Events

In the present study there were no severe AEs. The rate of AEs in this study is relatively high (7 of 11 participants reported an AE) compared to previous reports which suggest the risk of an AE occurring during RE to be about 5.5% (LaStayo et al., 2011; Lee et al., 2010; Musanti, 2012; Rajotte et al., 2012; Schmitz et al., 2005; Winters-Stone et al., 2012). It should be known that survivors in the present study were instructed to report all events that may occur whether inside or outside of the study regardless of severity. This may have elevated the rate of AE's in this study, even though only AEs resulting from RE are reported here.

Musculoskeletal injuries are known risks associated with RE and also occur in the general population. This risk may be reduced through supervision, paying attention to form when lifting, and moderate progression not exceeding increases in weight of more than 10% (ACSM, 2013; Heyward & Gibson, 2014). The aggravation of previous injuries made up modest portion of the AEs reported. These may have been prevented if more thorough screening procedures were used that ask participants about previous injuries and modification of exercises that may be problematic for those individuals. Given that the present study did show significant increases in muscular strength and endurance which are important outcomes for survivors' health and wellbeing, and the limited severity of the AEs that did occur, the efficacy of RE for survivors is still supported by this study.

Limitations

While the present study has shown that RE is an effective means for breast and ovarian cancer survivors to increase strength and that training frequency may influence the effectiveness

of strength training programs, it is not without its limits. The principle limitation of this study is its small sample size. Importantly, several key outcomes failed to reach statistical significance despite showing a large effect because they were underpowered. Also, given the small sample, we were unable to determine if ovarian cancer survivors responded to the intervention in a similar way as breast cancer survivors. Given the small sample, the present study handled missing data using the last observation carried forward method in an effort to preserve power. However, it is known that this increases the risk of committing a type I error. This is especially problematic when comparing the actual training frequency since all participants who dropped out from the study would be considered low actual training frequency.

Another problem encountered in the present study was the low adherence rate observed in the twice a week group. Given the small sample size it is not certain if poor adherence was the result of being in the higher frequency group or other unknown factors. Other studies (LaStayo et al., 2011; McKenzie & Kalda, 2003; Musanti, 2012; Rajotte et al., 2012; Schmitz et al., 2005; Winters-Stone et al., 2011) have used two and three days per week strength training frequencies and similar survivor groups and reported higher adherences ranging from 76-95%. These studies have found that survivors with poor adherence may share common traits including: beginning RE soon after diagnosis, poor mental health, difficulty performing activities of daily living, cancer related fatigue, obesity, and low physical activity levels. Comparisons between our high and low actual frequency groups revealed no significant differences.

A third limitation of this study was the lack of a control group. As mentioned, survivors in control groups in strength training studies may increase strength up to 12% without a strength training intervention as they recover from cancer treatment. In the present study, the average time since diagnosis was 5.5±8.4 years. The large variation in time since diagnosis, strength

gains as a result of treatment recovery does not fully account for improvements in strength seen here. Having a control group would allow for more definitive conclusions, particularly in regard to the effectiveness of the once-a-week protocol.

A fourth limitation comes from the lack of blinding that existed between group allocation, study supervision, and fitness testing. Although unintentional, expectations about the exercise interventions (that twice weekly RE is superior) may have affected the results of the study if encouragement was not kept consistent between groups during training or fitness testing. Attempts were made by the lead investigator supervising the sessions and conducting fitness tests (Mr. Gravelle) to maintain consistency between groups. During training Mr. Gravelle took a purely observational role when supervision provided by volunteers was adequate (i.e. not directly training survivors). Additionally, motivation was kept consistent during testing by keeping encouragement messages non-specific to the test (e.g. saying 'good' or 'you're doing fine' rather than 'you can do another rep'). These messages were given at regular intervals, every five repetitions during 1RM testing, and every ten repetitions during standard load tests. Regardless, the lack of blinding should be considered alongside the results of the present study.

Unfortunately the use of bioelectric impedance to assess body composition may have been a limitation in the present study. It is acknowledged that measuring body composition is difficult, especially when finding cost effective, non-invasive means for doing so. In the physical activity oncology literature, is has been seen that using less sophisticated technology to assess changes in body composition appears to coincide with null results. Like the present study, Rajotte et al (2012) was unable to detect changes in weight or waist circumference after 12 weeks of strength training in a community based program. To further this point, despite reporting

significant increases in lean body mass with decreases in body fat percentage, Schmitz et al. (2005) found no change in waist circumference after one year.

While bioelectric impedance satisfied the need for cost effective, non-invasive methods of measuring body composition, it has a unique problem of being influenced by the participants hydration status (Kushner et al., 1996). Because of this, bioelectric impedance analysis should be assessed in a fasted state, having nothing to eat or drink 8 hours prior (Kushner et al., 1996). When these conditions are not met, the standard measure of error can increase by as much as 4%. To help ensure this procedures were followed prior to testing, participants were reminded of these pre-testing conditions and testing was done in the morning. However, it was not uncommon for participants to comment that they needed to drink coffee in the morning or have breakfast. Testing was not canceled in these circumstances because it was felt that doing so would unnecessarily inconvenience the participants.

Future Directions

Several avenues for future research are evident. Certainly the effect of exercise frequency is just one aspect of an exercise prescription which may be varied to maximize outcomes or bring about certain training adaptations. How these specific adaptations affect day to day life of cancer survivors and how that in turn impacts QOL and fatigue is unknown and worth exploring. Related to this, some survivors may be able to train more effectively with different programs than others. For example, survivors coping with cancer related fatigue may find high repetition programs difficult and would prefer heavier low repetition programs, while survivors with osteoporosis may have limits on heavy lifting and need to perform more repetitions to compensate.

Increasing adherence to exercise interventions is another important avenue for future research. In the present study, attending one session or more per week was shown to have the greatest impact on muscular fitness, yet the twice-a-week group only attended 65% of their prescribed sessions. This unique finding highlights an interesting problem. Established dose-response relationships for strength training show that up to a certain point, increasing prescription variables such as training volume, intensity, and frequency also leads to greater increases strength development (Peterson et al., 2005). However, as the difficulty and time commitment to these programs increases it is reasonable to assume that adherence will decrease. For example, time is often cited as a barrier in physical activity studies of cancer survivors both on (Rogers et al., 2007) and off treatment (Courneya et al., 2005). As exercise frequency or training volume increases, the demands on a survivors time increase, this makes adherence more difficult. One possible solution is the use of single set protocols. While not shown to produce maximal strength gains (Rhea et al., 2003), single set protocols offer the possibility of building an adequate level of muscular fitness for daily living while minimizing time commitments (Carpinelli & Otto, 1999; Feigenbaum & Pollock, 1999; Messier & Dill, 1985).

Studies have also shown that self-efficacy is a strong predictor of exercise behavior and it has been reported that rural breast cancer survivors with higher task self-efficacy for exercise also perceived fewer barriers (Rogers, Markwell, Verhulst, McAuley, & Courneya, 2009). Group based exercise may be one way of increasing adherence as that format is more able to provide survivors with social support and modeling from similar others. Through self-efficacy, these positive group dynamics and social supports are thought to improve exercise adherence (Duncan & McAuley, 1993), yet this did not happen in the current study. Studies should investigate what qualities are needed to fully realize the benefits of group-based exercise (e.g., specific group

exercises, group discussions, team building experiences) and should do so based on existing behavioural models. Future studies should include self-efficacy measures, particularly when comparing exercise interventions; because of how poor adherence limits program efficacy.

Lastly, it was hoped that this study could be used to determine if gynecologic cancer survivors benefit from RE the same way as breast cancer survivors. Unfortunately, we were only able to recruit 4 gynecologic cancer survivors (all ovarian) making comparisons difficult.

Practical Applications

Based on the findings of the present study it is recommended that breast and ovarian cancer survivors begin strength training one to two days per week. The strength of this guideline is in its flexibility. It considers that some survivors have difficulty strength training twice-a-week and allows them to "miss a day" and still acquire health benefits and have mastery experiences (Bandura, 1994), ultimately promoting long term adherence. In the present study, survivors who strength trained at least once a week showed significant increases in upper and lower body strength with trends towards better physical functioning and fatigue.

Prescribing strength training once-a-week should be avoided, particularly given that minimum targets are frequently under achieved. Despite the present study showing that the once-a-week group also showed improvements in muscular fitness, these gains were small and not appreciably different from control groups seen throughout the literature (Musanti, 2012; Ohira et al., 2006; Rajotte et al., 2012; Schmitz et al., 2009; Schmitz et al., 2005; Winters-Stone et al., 2012). Additionally, prescribing strength training once-a-week does not provide any buffer for missing sessions. If an exercise program for survivors is only offered once-a-week and a session is missed, the time period between bouts of exercise would be two weeks. Keep in mind, that if all a survivor is able to do is train once-a-week, the small benefits in strength (or at the very least

preservation of muscular fitness) are still valuable given that the expectation later in life is a decline (Kallman et al., 1990).

It should be mentioned that delivery of this exercise program was not only feasible but it was also beneficial to the local community as well. The program was implemented with minimal costs, using exercise equipment already existing in the hospital setting and supervised by student volunteers and researchers. Not only did this provide a chance for breast and ovarian cancer survivors to engage in beneficial exercise, it also supported research and helped undergraduate students acquire valuable learning experiences. This may be a beneficial model to base future cancer rehabilitation programs on in the future, but it may be improved upon. The ridged schedule of the present study meant survivors were not free to exercise when they chose. This may have had an unintentionally negatively influenced autonomy, and in turn, adherence. This was done because of the limited availability of the study's exercise physiologist. Having more flexible times when survivors may come in for exercise would, therefore, be a more practical way of enhancing adherence.

Conclusion

This is the first study of its kind to directly examine the effect of training variables in a cancer population after treatment by comparing once and twice-a-week strength training. The results of this study support previous findings that strength training is a safe and effective means of increasing muscular strength and endurance in cancer survivors. It is recommended that survivors should begin strength training one to two times per week, with an added emphasis on training twice-a-week if possible.

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Appendix A

Ethical Approval

Capital Health

Capital Health Research Ethics Board
Centre for Clinical Research, Room 118
5790 University Avenue
Halifax, Nova Scotia, Canada B3H 1V7
Phone: 473-5639 Fax: 473-5620

November 08, 2012

Dr. Scott Grandy
Health Professions\Health & Human Performance
6230 South Street
Halifax ,NS
B3H 1T8

Full Board Review
Full Approval Letter
(October 15, 2012 to October 15, 2013)

ATTENTION: Mr. Tim Gravelle

Dear Dr. Grandy:

RE: Exercise Frequency in Breast and Gynecological Survivors

REB FILE #: CDHA-RS/2013-157

Thank you for your response received November 08, 2012 regarding your proposed study.

Document Name	Comments	Version Date
Cover Letter • *Signed by Tim Gravelle*	n/a	Not Dated
Researcher's Checklist for Submissions • *Signed by Dr. Scott Grandy*	n/a	07 Nov 2012
Ethics Approval Submission Form • *Signed by Dr. Scott Grandy*	n/a	07 Nov 2012
Consent Form	2.0	25 Aug 2012
Research Team Contact page	2.0	25 Aug 2012
Research Protocol • Appendix G – Study Design	n/a n/a	Not Noted Not Noted
Advertisement(s): • "Happiness? Confidence? Strength?"	2.0	25 Aug 2012

Healthy People, Healthy Communities

I have reviewed these documents on behalf of the Research Ethics Board (REB) and note that all requested changes have been incorporated.

I am now pleased to confirm the Board's full approval for this research study, effective today. This includes approval / favourable opinion for the following study documents:

Document Name	Version No.	Version Date
Cover Letter • *Signed by Tim Gravelle*	n/a	Not Dated
Researcher's Checklist for Submissions • *Signed by Dr. Scott Grandy*	n/a	07 Nov 2012
Letter of Support from the Principal Investigator's Department/Division/ Program/Service • *Signed by Fred McGinn*	n/a	25 Aug 2012
Letter of Support from the Site Investigator's Department/Division/Program/Service • *Signed by S. Jackson*	n/a	28 Aug 2012
Ethics Approval Submission Form • *Signed by Dr. Scott Grandy*	n/a	07 Nov 2012
Consent Form	2.0	25 Aug 2012
Research Team Contact page	2.0	25 Aug 2012
Supporting Material(s): • The Risk Stratification Questionnaire • Interpretation of the Risk Stratification Questionnaire • PARmed-X • Getting to Know You Questionnaire • Leisure Time Exercise Questionnaire • FACT-F • The Medical Outcomes Survey Questionnaire • Checking In – Leisure Time Exercise Questionnaire • Strength Training Program – Booklet	 1 1 1.0 1.0 1.0 4 1.0 1.0 1.0	 Not Dated Not Dated 2002 Not Dated Not Dated Not Dated ©1992-2002 Not Dated Not Dated
Advertisement(s): • "Happiness? Confidence? Strength?"	2.0	25 Aug 2012
Protocol	n/a	Not Dated
Principal investigator's TCPS2: Core Certificate of Completion		27 Aug 2012
Principal investigator's Current CV		05 Sep 2012

Continuing Review

1. **The Board's approval for this study will expire one year after the date of full Board review (October 15, 2013).** To ensure continuing approval, submit a Request for Annual Approval to the Board 2-4 weeks prior to this date. If approval is not renewed prior to the

anniversary date, the Board will close your file and you must cease all study activities immediately. To reactivate a study, you must submit a new Initial Submission (together with the usual fee) to the REB and await notice of reapproval.
2. Please be sure to notify the Board of any:
- Proposed changes to the initial submission (i.e., new or amended study documents),
- Additional information to be provided to study participants,
- Material designed for advertisement or publication with a view to attracting participants,
- Serious adverse events experienced by local participants,
- Unanticipated problems involving risks to participants or others,
- Sponsor-provided safety information (e.g., reports of serious unexpected adverse reactions, changes to the investigator's brochure / product monograph, DSMB reports)
- Additional compensation available to participants,
- Upcoming audits / inspections by a sponsor or regulatory authority,
- Closure of the study (within 90 days of the event).
3. Approved studies may be subject to internal audit. Should your research be selected for audit, the Board will advise you and indicate any other requests at that time.

Important Instructions and Reminders

1. Submit all correspondence to Ethics Coordinator, Starla Burns at the address listed at the top of this letter (do not send your response to the REB Chair or Co-Chair).
2. Be sure to reference the Board's assigned file number, CDHA-RS/2013-157, on all communications.
3. Highlight all changes on revised documents, and remember to update version numbers and/or dates.
4. If you plan to advertise in a newspaper, send the REB-approved advertisement to dragan.samardic@cdha.nshealth.ca for placement in the appropriate CDHA template.

Best wishes for a successful study.

This statement is in lieu of Health Canada's Research Ethics Board Attestation:
The Research Ethics Board for the Capital District Health Authority operates in accordance with:
- *Food and Drug Regulations, Division 5 "Drugs for Clinical Trials Involving Human Subjects"*
- *Natural Health Products Regulations, Part 4 "Clinical Trials Involving Human Subjects"*
- *ICH Good Clinical Practice: Consolidated Guideline (ICH-E6)*
- *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*
- *Titles 21 and 45, U.S. Code of Federal Regulations.*

/sb

Appendix B

Consent Form

Consent Form

Consent Form

STUDY TITLE: Exercise Frequency in Breast and Gynecological Cancer Survivors

CLINICAL TRIALS REGISTRY: ClinicalTrials.gov NCT01709175

PRINCIPAL INVESTIGATOR: Dr. Scott Grandy
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Email: scott.grandy@dal.ca
Address: School of Health and Human Performance
Dalhousie University
6230 South Street
PO Box 15000
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ASSOCIATE INVESTIGATORS: Please see the attached Research Team Contact Page for a full list of the investigators for this trial.

PART A: GENERAL INFORMATION

1. Introduction

You have been invited to take part in a research study. Taking part in this study is voluntary. It is up to you to decide whether to be in the study or not. Before you decide, you need to understand what the study is for, what risks you might take and what benefits you might receive. This consent form explains the study.

Please read this carefully. Take as much time as you like. If you like, take it home to think about for a while. Mark anything you don't understand, or want explained better. After you have read it, please ask questions about anything that is not clear.

The researchers will:

- Discuss the study with you
- Answer your questions
- Keep confidential any information which could identify you personally; and
- Be available during the study to deal with problems and answer questions

We do not know if taking part in this study will help you. You may feel better. On the other hand it might not help you at all. It might even make you feel worse. We cannot always predict these things. We will always give you the best possible care no matter what happens.

If you decide not to take part or if you leave the study early, your usual health care will not be affected.

PART B: EXPLAINING THIS STUDY

2. Why is this study being done?

Studies have shown that breast and gynecological survivors experience decreased fitness and quality of life as a result of their disease or its treatment. Studies have also shown that exercise has the potential to improve quality of life, fitness, and fatigue in survivors. However, little is known about what resistance exercise (strength training by lifting weights) or what kinds of strength training programs are the most effective. The purpose of this study is to examine the potential of strength training to improve health outcomes. This study will also compare two different strength programs to provide a better understanding of what types of programs are best for survivors.

3. What Is Being Tested?

This study will be testing two different exercise programs (once-a-week vs. twice-a-week) to determine which is optimal for breast and gynecologic cancer survivors. It is hoped that this

study will help strengthen our understanding of strength training in this population and help inform future exercise guidelines for survivors.

4. Why Am I Being Asked To Join This Study?

You are being asked to join this study because you are a survivor of breast or gynecological cancer and you have expressed interest in participating.

5. How Long Will I Be In The Study?

This is a 13-week long study. If you decide to participate you will be invited to attend either one or two sessions of strength training each week. The number of sessions you will be asked to attend each week will be determined by randomized group assignment (i.e., by chance, similar to flipping a coin). Each session of strength training is expected to last 90 minutes. You will also be asked to have 3 fitness assessments done (on a separate day from strength training) and hand in a completed survey at each assessment (baseline, week-7, week-13). Each fitness assessment will take approximately 30 minutes to complete, and each survey will take an additional 15 minutes (done at home and handed in when you do the fitness assessment).

6. How Many People Will Take Part In This Study?

This study is being done in Halifax, Nova Scotia. A total of 20 people are anticipated to participate in this study, although your exercise group may be smaller than this. Participants will be randomly assigned to one of two groups. The first group will be offered strength training once a week; the second group will be offered the same program but twice a week. Group size will depend on how many people are enrolled in the study at the time and could be as small as four (4) people or as large as 10.

7. How Is The Study Being Done?

Adult survivors of breast and gynecological cancer will be recruited primarily from the Halifax area, although women from other parts of the province may also wish to participant. If you agree to participate in this study, you will be asked to:

1. Sign and return a copy of this consent form;
2. Complete the enclosed baseline survey; and
3. Have your physician complete the PARMed-X and risk stratification questionnaires.

Once we have received this information, you will be asked to participate in a one week introduction to strength training program. This will be done for two days spread over the first week of the program and will familiarize everyone with the program that is being offered. At the end of this week there will be a baseline fitness assessment. Once this is completed, you will be randomly selected to receive one of two strength training programs. The only difference between these programs is how often you attend the sessions (either once or twice a week). Your role in this study will involve following this exercise program for the next 12 weeks to the best of your ability and to completing the fitness assessments and surveys that will be done in the middle (week 7) and at the end of the program (week 13). The strength training program, which is being supervised by a certified exercise physiologist and a female exercise instructor, will last for 12 weeks and each session will last about 90 minutes. Participation is voluntary, but you will be

encouraged to attend as many of your assigned sessions as possible. You will also be given a log book to record what you do during each exercise session.

8. What Will Happen If I Take Part In This Study?

If you want to be in this study and sign this consent form, you will be asked to have some tests done to see if you can take part. This is called screening. It is possible that the tests will show that you can't be in the study. There may be other tests done as part of usual care. The research team will discuss these with you. The research study screening tests that will be done are: physician completed PARMed-X and risk stratification questionnaire. These are simple tools that will help ensure that it is safe for you to participate in a strength training program. You will be asked to return the signed medical clearance forms, signed consent forms, and baseline surveys. After we receive these forms you will be asked to participate in an introduction to strength training and complete a baseline fitness assessment. The fitness assessment includes two strength tests which will require you to lift some weights on a bench press and a leg press to test your muscular strength and endurance. This assessment also includes an assessment of your body composition and will measure your height, weight, percent body fat and amount of lean body mass. After which you will be randomly assigned a strength training program. There is no difference between these programs other than how often you participate in the exercise sessions (either once or twice a week). You will be asked to attend the supervised strength training classes for the remaining 12 weeks of the program. These sessions will begin and end with a light aerobic warm-up/cool down. Over the course of the study, you will be asked to complete two follow-up assessments (week 7 and week 13). In total you will have completed 3 fitness assessments, 3 surveys, and a log book during your participation. All study materials (surveys and exercise log books) will be given to you directly at the lab before or after your exercise session. The exercise log book includes descriptions of the exercises we would like for you to do and recording sheets for you and the research team to keep track of your progress and ability to do the exercise program. If at any during the study you change your mind and decide you no longer wish to participate, you may withdraw at any time without explanation.

In brief, if you agree to participate in this study, you will need to:

- Have your physician complete and sign the PARMed-X and risk stratification questionnaire;
- Sign and return a copy of this consent form;
- Complete a brief survey before starting the strength training program;
- If you are still eligible for the study, attend as many of the 90-minute strength sessions as you are able; and
- Complete the fitness assessments and surveys at baseline, week 7 and week 13

Description of Assessments

Each assessment (baseline, week 7, and week 13) includes the following tests. Note that for each assessment your participation is voluntary and you can refuse any test.

Predicted One Repetition Maximum Strength Test

This test is used to measure the strength of your upper (e.g., arms) and lower (e.g., legs) body and provides an estimate of the heaviest weight you can lift one time (called 1RM). You will be asked to warm-up by performing 6 to 10 repetitions on the bench press (upper body exercise) and

leg press (lower body exercise) with a weight that is estimated to be 50% of your 1RM (recall that 1RM is an estimate of the heaviest weight you can lift one time). After a brief rest (approximately two minutes), you will be asked to perform as many repetitions as possible with a weight that you should not be able to do more than 10 repetitions with. If you are able to do more than 10 reps than you will be asked to take another brief rest and perform the exercise again with a heavier weight. If you are still able to do more than 10 repetitions at this point you will be asked to repeat the exercise one last time.

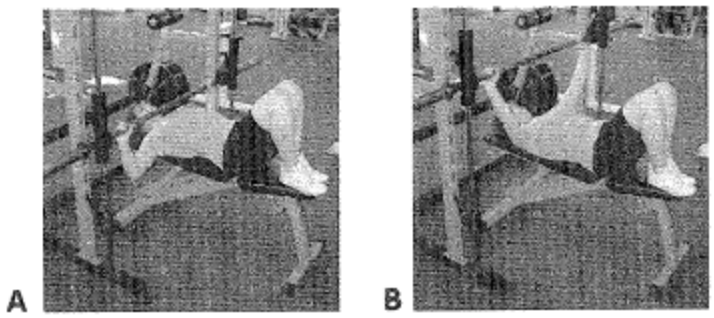


Figure 1. The bench-press exercise, used in the one repetition maximum and standard load tests.

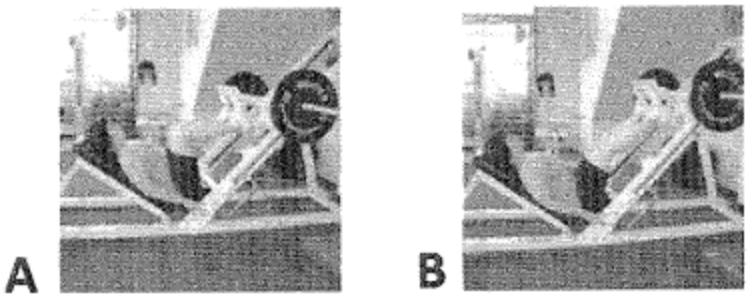


Figure 2. The leg press, used in the one repetition maximum and standard load tests.

Body Composition

Testing body composition will provide the researcher with information about how the strength training intervention affects the proportion of lean muscle and fat in your body. This will be determined using bioelectric impedance. Bioelectrical impedance determines body composition by sending a weak electrical signal through your body (this is painless) and measuring how long it takes the signal to return to the analyzer. You will be asked to stand on the analyzer in your bare feet and your height will also be measured. Having your body composition assessed with bioelectrical impedance is very similar to weighting yourself on a bathroom scale.

Standard Load Test

This test is used to measure muscular endurance, the amount of work you can do with your muscles before the fatigue. For this test you will be asked to perform as many repetitions as possible one the bench press and leg press with a weight that determined to be 50% of your one repetition maximum (calculated from the earlier predicted one repetition maximum test).

Quality of Life

Quality of life will be determined using the Medical Outcomes Survey – Short Form. This survey asks 36 questions related to your physical well-being, bodily-pain, general health, vitality, social functioning, and mental well-being.

Fatigue

The extent and severity of your fatigue will be determined using the Functional Assessment of Cancer Treatment – Fatigue Scale. This is a 13 item questionnaire that asks you to rank statements, such as "I feel fatigued", on how well they describe you.

Additional Responsibilities

It is important that you tell the principal Investigator about any drugs or medicines you are taking or wish to take. You must also tell the principal Investigator if you become pregnant or about anything unusual that is happening with your health. This includes any medical problems that seem to be getting worse. If you have to see another doctor or have to go to a hospital, you must let the doctors know that you are in a research study. You should also tell your own doctor as quickly as possible, for your safety.

9. What About Birth Control and Pregnancy?

If you get pregnant during the study you will be asked to stop participating in the study. This is because the exercise program used in this study would need to be changed to better suit the needs of a pregnant woman. Additionally, the fitness tests may be affected by pregnancy as procedures may need to be changed and the accuracy of the tests may be lowered.

10. Are There Risks To The Study?

As with any physical activity program or study there are some risks. To give you the most complete information available, we have listed the *possible* risks, which may appear alarming. We do not want to alarm you but we do want to make sure that you have had a chance to think about all the risks carefully before you choose to participate. Please also be aware that there may be risks in participating in this study that we do not know about yet.

Strength training studies have shown that a very common side-effect of strength training for both cancer survivors as well as those without cancer is muscle soreness and stiffness (approximately 1 or more out of every in 10 people experience this). This is more likely to occur when you begin your program, but is minimized by the introduction to strength training which is a less intense version of the program you will be doing. There is also a rare chance (approximately 1 or more out of every 10,000 people) that you could have a seizure. To reduce this risk, we are excluding persons who have had brain metastasis or seizures. In instances where someone has experienced muscle soreness or a seizure they have been able to fully recover from these events. In the event

that someone does become injured or suddenly ill both the Exercise Physiologist and the exercise instructor are trained in CPR and first aid and can provide emergency care. It will be your responsibility to report any injuries or illnesses that occur during the time of the study (even those that occur outside the program).

In addition to the strength training program, you will be asked to complete three surveys (one at each assessment). These surveys will ask you questions about your quality of life, your current level of physical activity, and experience with fatigue. If you are uncomfortable in responding to any of these questions you can leave them blank or you are free to withdraw from the study without penalty.

Lastly, as you will be strength training with a group of other women it is impossible to ensure your privacy. Other participants in this study will know about your participation.

11. Are There Other Choices?

You are free to seek other opinions or choices if you wish. You do not have to participate in this trial to begin a strength training program or to become physically active. You may choose to speak with your physician, oncologist, or a qualified fitness expert about strength training.

12. What Happens at the End of the Study?

This study is being conducted to better understand how strength training can benefit cancer survivors. If you would like a summary of the results, please notify the primary investigator and a summary will be mailed or emailed to you upon completion of the study. Should you be interested in learning more about the strength training or physical activity options in your area, we encourage you to speak to your physician, oncologist, or a certified fitness professional.

13. What Are My Responsibilities?

As a study participant you will be expected to:

- Follow the directions of the Principal Investigator
- Report all medications being taken or that you plan on taking
- Report any changes in your health to the Principal Investigator
- Report any problems that you experience that you think might be related to participating in the study
- Read this consent form before you sign it
- Have your physician complete the PAR Med-X and risk stratification questionnaire;
- Return the signed consent form, signed PAR Med-X, and completed the baseline surveys to the research team
- Follow the 13-week strength training program that is randomly assigned to you to the best of your ability
- Complete the fitness assessments and follow-up surveys at the end of weeks 1, 7 and 13
- Report any changes to your health during the time of the study (even those occurring outside of the study) to the principal investigator including: injuries, illnesses, and if you become pregnant; and to follow the directions of the Principal Investigator and research team

14. Can I Be Taken Out Of The Study Without My Consent?

While unlikely, you may be removed by the study's Principal Investigator or the Research Ethics Board from the study at anytime if:

- There is new information that shows being in this study is not in your best interest;
- You are experiencing side-effects that are harmful to your health or well-being;
- You are not following the directions of the Principal Investigator or research team;
- You become pregnant;
- The Principal Investigator, Capital Health Research Ethics Board, or your doctor, decides to stop the study.

You will be told about the reasons why you might need to come out of the study.

15. What About New Information?

It is possible that new information may become available while you are in the study that might affect your health, welfare, or willingness to stay in the study. If this happens you will be informed in a timely manner and will be asked whether you wish to continue taking part in the study.

16. Will It Cost Me Anything?

Compensation

You will not be paid to be in this study. We are not charging for the study or for any materials you receive. However, your physician will require payment for completing the PARMed-X and Risk questionnaires and you may also have to pay for your transportation and parking. We cannot reimburse you for these costs or any other cost you may incur as a result of participating in this study.

Research Related Injury

If you become ill or injured as a direct result of participating in this study, necessary medical treatment will be available at no additional cost to you. Your signature on this form only indicates that you have understood to your satisfaction the information regarding your participation in the study and agree to participate in the study. In no way does this waive your legal rights nor release the Principal Investigator, the research team, the study sponsor or involved institutions from their legal and professional responsibilities.

17. What About My Privacy and Confidentiality?

Protecting your privacy is an important part of this study. Every effort to protect your privacy will be made. However, complete privacy cannot be guaranteed. Since you will be in an exercise group other participants will know about your involvement in this study. Also, as we require you to get medical clearance from your physician, they will know you are taking part in the study. We cannot guarantee your privacy if the research team is required by law to allow access to this study's records. A copy of this consent form will be put in your health record.

To protect your privacy no identifying information (such as your name or hospital number) will be shared with anyone outside of the research team. If the results of this study are presented to the public, nobody will be able to tell that you were in the study.

When you sign this consent form, you give us permission to:

- Collect information from you;
- Share information with the people conducting the study; and
- Share information with the people responsible for protecting your safety while participating in this research.

Access to Records and Use of Records

The research team will not access or collect any data from your personal health records. The research team will collect and use only the information they need to judge the safety and usefulness of the exercise intervention. Members of the research team may need to see study records that identify you by name. All hard copies of surveys and results from fitness tests collected from this study will be kept in a locked cabinet in Dr. Melanie Keats' faculty office (Office 216C within the Dalplex building at Dalhousie University). All electronic copies will be stored on one encrypted, password protected hard drive. Both hard and electronic copies of your information will be securely stored for 7 years after the publication of the results from the study, at which point all physical and electronic data from this study will be destroyed.

Your Access to Records

You may ask the research team to see the information that has been collected about you. You may ask to make corrections to this information by talking with a member of the research team.

18. What If I Want To Quit The Study?

If you chose to participate and later change your mind, you can say no and stop your participation at any time. If you wish to leave the study please inform a member of the research team. A decision to stop participating in the study will not affect your health care. All data collected up to the date you withdraw your consent will remain in the study records, to be included in study related analyses.

20. Declaration of Financial Interest

There is no payment being received by the Principal Investigator or the research team for conducting this study. Neither the Principal Investigator nor the Research Team has a financial interest in conducting this study.

21. What About Questions Or Problems?

For further information about the study call **Tim Gravelle OR Dr. Melanie Keats.** Mr. Gravelle's work telephone number is (902) 209-3983, and Dr. Keats' work telephone number is (902) 494-7173. Scott Grandy may be contacted by phone at (902) 494-1145. All contact numbers are secure and only the research team has access. If you cannot reach Mr. Gravelle or

Dr. Keats, please refer to the attached Research Team Contact Page for a full list of the people you can contact for further information about the study. Tim Gravelle can be contacted after hours using his work phone number.

If you experience any symptoms or possible side effects or other medical problems, please let the Mr. Gravelle or Dr. Keats know immediately.

22. What Are My Rights?

Two copies of the consent form have been provided for you in your introductory package. Please sign both consent forms, keep one for your records and return the other with the physician signed PARMed-X and Risk Stratification questionnaires, and baseline survey.

If you have any questions about your rights as a research participant, contact the **Patient Representative** at **(902) 473-2133.**

In the next part you will be asked if you agree (consent) to join this study. If the answer is "yes", you will need to sign the form.

PART C: Consent Form Signature Page

I have reviewed all of the information in this consent form related to the trial called:

Exercise Frequency in Breast and Gynecological Cancer Survivors

I have been given the opportunity to discuss this study and all of my questions have been answered to my satisfaction.

I agree that my personal health and study information may be used as described in this consent form.

This signature on this consent form means that I agree to take part in this study. I understand that I am free to withdraw at any time without affecting my future care.

_____ Signature of Participant	_____ Name (Printed)	____ / ____ / ____ Year Month Day*
_____ Witness to Participant's Signature	_____ Name (Printed)	____ / ____ / ____ Year Month Day*
_____ Signature of Investigator	_____ Name (Printed)	____ / ____ / ____ Year Month Day*
_____ Signature of Person Conducting Consent Discussion	_____ Name (Printed)	____ / ____ / ____ Year Month Day*

Note: Please fill in the dates personally

Please sign both copies of the consent form. Keep one copy for your records and return the second to the research team.

Thank you for your time and patience!

Appendix C

Research Team Contact Page

Capital Health

Research Team Contact Page

Exercise Frequency in Breast and Gynecological Cancer Survivors				
Name	**Role**	**Work Address**	**Telephone Number**	**E-Mail Address**
Dr. Scott Grandy	Principle Investigator	School of Health and Human Performance, Dalhousie University 6230 South Street PO Box 15000 Halifax, NS B3H 4R2	(902) 494-1145	scott.grandy@dal.ca
Dr. Melanie Keats	Investigator	School of Health and Human Performance, Dalhousie University 6230 South Street Halifax, NS B3H 1T8	(902) 494-7173	melanie.keats@dal.ca
Mr. Tim Gravelle	Investigator	School of Health and Human Performance, Dalhousie University 6230 South Street Halifax, NS B3H 1T8	(902) 580-9494	tim.gravelle@dal.ca
Dr. Chris Blanchard	Investigator	Dept. of Medicine, Dalhousie University Centre for Clinical Research – Suite 205 5790 University Avenue Halifax, NS, B3H 1V7	(902) 473-3789	chris.blanchard@dal.ca

Appendix D

Recruitment Poster

DALHOUSIE UNIVERSITY
Inspiring Minds

Capital Health

Happiness? Confidence? Strength?

What will you Develop?

IF YOU ARE...

- ✓ 18 OR OLDER
- ✓ HAVE SURVIVED BREAST OR GYNECOLOGICAL CANCER
- ✓ AND HAVE NOT BEEN STRENGTH TRAINING IN THE PAST 6 MONTHS

YOU MAY QUALIFY FOR A STRENGTH TRAINING STUDY.

WE ARE OFFERING BREAST AND GYNECOLOGICAL CANCER SURVIVORS A 13-WEEK STRENGTH TRAINING PROGRAM TO EXPLORE HOW STRENGTH TRAINING AFFECTS THE FITNESS AND QUALITY OF LIFE OF SURVIVORS.

WANT TO LEARN MORE? PLEASE CONTACT TIMOTHY GRAVELLE AT TIM.GRAVELLE@DAL.CA OR CALL 1 (902) 580-9494.

CDHA-RS/2013-157 2013/10/2 – Version 2.1

Appendix E

Risk Assessment Questionnaires

Risk Stratification Questionnaire

Part 1. To be completed by your physician.

Please answer the following questions to the best of your ability. If more room is needed please use the back of the sheet.

1) Is this person a female survivor of breast or gynecologic cancer and have they completed primary cancer treatment (except for hormone based therapies such as *Tamoxifen*)?
   ▫Yes ▫ No

2) Has this person been diagnosed with another chronic condition or have a history of seizures, if so please indicate which ones or if you are unsure
   _____
   _____

3) Has this person had or currently have one of the following types of cancer?
   ▫Any lung cancers ▫Multiple Myeloma ▫Cancer of the head and neck
   ▫Unsure

4) Are they currently on any cancer treatments? If so please indicate which ones (include all hormone based cancer treatments).
   _____
   _____

5) Did this person's cancer treatment include chemotherapy?
   ▫Yes ▫No

6) Is this person currently on any other medication? If so please list them and if any changes in medication have occurred in the past 30 days.
   _____
   _____

7) Are the results of this person's last tests normal?
   ▫Yes ▫No ▫Unknown

I am _____'s physician and I have answered the above questions to the best of my ability.
X_____ Date_____

Part 2. To be completed by the participant.

8) Have you been doing a structured strength training program in the past six months?
   ▫ Yes ▫ No

Physical Activity Readiness
Medical Examination
(revised 2002)

PARmed-X PHYSICAL ACTIVITY READINESS MEDICAL EXAMINATION

The PARmed-X is a physical activity-specific checklist to be used by a physician with patients who have had positive responses to the Physical Activity Readiness Questionnaire (PAR-Q). In addition, the Conveyance/Referral Form in the PARmed-X can be used to convey clearance for physical activity participation, or to make a referral to a medically-supervised exercise program.

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. The PAR-Q by itself provides adequate screening for the majority of people. However, some individuals may require a medical evaluation and specific advice (exercise prescription) due to one or more positive responses to the PAR-Q.

Following the participant's evaluation by a physician, a physical activity plan should be devised in consultation with a physical activity professional (CSEP Certified Exercise Physiologist®. To assist in this, the following instructions are provided:

PAGE 1: • Sections A, B, C, and D should be completed by the participant BEFORE the examination by the physician. The bottom section is to be completed by the examining physician.

PAGES 2 & 3: • A checklist of medical conditions requiring special consideration and management.

PAGE 4: • Physical Activity & Lifestyle Advice for people who do not require specific instructions or prescribed exercise.

• Physical Activity Readiness Conveyance/Referral Form - an optional tear-off tab for the physician to convey clearance for physical activity participation, or to make a referral to a medically-supervised exercise program.

This section to be completed by the participant

A PERSONAL INFORMATION:

NAME _____

ADDRESS _____

_____

TELEPHONE _____

BIRTHDATE _____ GENDER _____

MEDICAL No. _____

B PAR-Q: Please indicate the PAR-Q questions to which you answered YES

- ❑ Q 1 Heart condition
- ❑ Q 2 Chest pain during activity
- ❑ Q 3 Chest pain at rest
- ❑ Q 4 Loss of balance, dizziness
- ❑ Q 5 Bone or joint problem
- ❑ Q 6 Blood pressure or heart drugs
- ❑ Q 7 Other reason:

_____

C RISK FACTORS FOR CARDIOVASCULAR DISEASE:

Check all that apply

- ❑ Less than 30 minutes of moderate physical activity most days of the week.
- ❑ Currently smoker (tobacco smoking 1 or more times per week).
- ❑ High blood pressure reported by physician after repeated measurements.
- ❑ High cholesterol level reported by physician.
- ❑ Excessive accumulation of fat around waist.
- ❑ Family history of heart disease.

***Please note:** Many of these risk factors are modifiable. Please refer to page 4 and discuss with your physician.*

D PHYSICAL ACTIVITY INTENTIONS:

What physical activity do you intend to do?

_____

_____

_____

This section to be completed by the examining physician

Physical Exam:

Ht	Wt	BP i) /
		BP ii) /

Conditions limiting physical activity:

- ❑ Cardiovascular
- ❑ Musculoskeletal
- ❑ Respiratory
- ❑ Abdominal
- ❑ Other

Tests required:

- ❑ ECG
- ❑ Blood
- ❑ Exercise Test
- ❑ Urinalysis
- ❑ X-Ray
- ❑ Other

Physical Activity Readiness Conveyance/Referral:

Based upon a current review of health status, I recommend:

Further Information:
- ❑ Attached
- ❑ To be forwarded
- ❑ Available on request

- ❑ No physical activity
- ❑ Only a medically-supervised exercise program until further medical clearance
- ❑ Progressive physical activity:
  - ❑ with avoidance of: _____
  - ❑ with inclusion of: _____
  - ❑ under the supervision of a CSEP Certified Exercise Physiologist®
- ❑ Unrestricted physical activity–start slowly and build up gradually

Supported by: Health Canada Santé Canada

Physical Activity Readiness
Medical Examination
(revised 2002)

PARmed-X PHYSICAL ACTIVITY READINESS MEDICAL EXAMINATION

Following is a checklist of medical conditions for which a degree of precaution and/or special advice should be considered for those who answered "YES" to one or more questions on the PAR-Q, and people over the age of 69. Conditions are grouped by system. Three categories of precautions are provided. Comments under Advice are general, since details and alternatives require clinical judgement in each individual instance.

	Absolute Contraindications	Relative Contraindications	Special Prescriptive Conditions	ADVICE
	Permanent restriction or temporary restriction until condition is treated, stable, and/or past acute phase.	Highly variable. Value of exercise testing and/or program may exceed risk. Activity may be restricted. Desirable to maximize control of condition. Direct or indirect medical supervision of exercise program may be desirable.	Individualized prescriptive advice generally appropriate: • limitations imposed; and/or • special exercises prescribed. May require medical monitoring and/or initial supervision in exercise program.	
Cardiovascular	❑ aortic aneurysm (dissecting) ❑ aortic stenosis (severe) ❑ congestive heart failure ❑ crescendo angina ❑ myocardial infarction (acute) ❑ myocarditis (active or recent) ❑ pulmonary or systemic embolism—acute ❑ thrombophlebitis ❑ ventricular tachycardia and other dangerous dysrhythmias (e.g., multi-focal ventricular activity)	❑ aortic stenosis (moderate) ❑ subaortic stenosis (severe) ❑ marked cardiac enlargement ❑ supraventricular dysrhythmias (uncontrolled or high rate) ❑ ventricular ectopic activity (repetitive or frequent) ❑ ventricular aneurysm ❑ hypertension—untreated or uncontrolled severe (systemic or pulmonary) ❑ hypertrophic cardiomyopathy ❑ compensated congestive heart failure	❑ aortic (or pulmonary) stenosis—mild angina pectoris and other manifestations of coronary insufficiency (e.g., post-acute infarct) ❑ cyanotic heart disease ❑ shunts (intermittent or fixed) ❑ conduction disturbances • complete AV block • left BBB • Wolff-Parkinson-White syndrome ❑ dysrhythmias—controlled ❑ fixed rate pacemakers	• clinical exercise test may be warranted in selected cases, for specific determination of functional capacity and limitations and precautions (if any). • slow progression of exercise to levels based on test performance and individual tolerance. • consider individual need for initial conditioning program under medical supervision (indirect or direct).
			❑ intermittent claudication	progressive exercise to tolerance
			❑ hypertension: systolic 160-180; diastolic 105+	progressive exercise; care with medications (serum electrolytes; post-exercise syncope; etc.)
Infections	❑ acute infectious disease (regardless of etiology)	❑ subacute/chronic/recurrent infectious diseases (e.g., malaria, others)	❑ chronic infections ❑ HIV	variable as to condition
Metabolic		❑ uncontrolled metabolic disorders (diabetes mellitus, thyrotoxicosis, myxedema)	❑ renal, hepatic & other metabolic insufficiency	variable as to status
			❑ obesity ❑ single kidney	dietary moderation, and initial light exercises with slow progression (walking, swimming, cycling)
Pregnancy		❑ complicated pregnancy (e.g., toxemia, hemorrhage, incompetent cervix, etc.)	❑ advanced pregnancy (late 3rd trimester)	refer to the "PARmed-X for PREGNANCY"

References:

Arraix, G.A., Wigle, D.T., Mao, Y. (1992). Risk Assessment of Physical Activity and Physical Fitness in the Canada Health Survey Follow-Up Study. **J. Clin. Epidemiol.** 45:4 419-428.

Mottola, M., Wolfe, L.A. (1994). Active Living and Pregnancy, In: A. Quinney, L. Gauvin, T. Wall (eds.), **Toward Active Living: Proceedings of the International Conference on Physical Activity, Fitness and Health**. Champaign, IL: Human Kinetics.

PAR-Q Validation Report, British Columbia Ministry of Health, 1978.

Thomas, S., Reading, J., Shephard, R.J. (1992). Revision of the Physical Activity Readiness Questionnaire (PAR-Q). **Can. J. Spt. Sci.** 17: 4 338-345.

Continued on page 3...

	Special Prescriptive Conditions	ADVICE
Lung	❑ chronic pulmonary disorders	special relaxation and breathing exercises
	❑ obstructive lung disease ❑ asthma	breath control during endurance exercises to tolerance; avoid polluted air
	❑ exercise-induced bronchospasm	avoid hyperventilation during exercise; avoid extremely cold conditions; warm up adequately; utilize appropriate medication.
Musculoskeletal	❑ low back conditions (pathological, functional)	avoid or minimize exercise that precipitates or exasperates e.g., forced extreme flexion, extension, and violent twisting; correct posture, proper back exercises
	❑ arthritis—acute (infective, rheumatoid; gout)	treatment, plus judicious blend of rest, splinting and gentle movement
	❑ arthritis—subacute	progressive increase of active exercise therapy
	❑ arthritis—chronic (osteoarthritis and above conditions)	maintenance of mobility and strength; non-weightbearing exercises to minimize joint trauma (e.g., cycling, aquatic activity, etc.)
	❑ orthopaedic	highly variable and individualized
	❑ hernia	minimize straining and isometrics; stregthen abdominal muscles
	❑ osteoporosis or low bone density	avoid exercise with high risk for fracture such as push-ups, curl-ups, vertical jump and trunk forward flexion; engage in low-impact weight-bearing activities and resistance training
CNS	❑ convulsive disorder not completely controlled by medication	minimize or avoid exercise in hazardous environments and/or exercising alone (e.g., swimming, mountainclimbing, etc.)
	❑ recent concussion	thorough examination if history of two concussions; review for discontinuation of contact sport if three concussions, depending on duration of unconsciousness, retrograde amnesia, persistent headaches, and other objective evidence of cerebral damage
Blood	❑ anemia—severe (< 10 Gm/dl) ❑ electrolyte disturbances	control preferred; exercise as tolerated
Medications	❑ antianginal ❑ antiarrhythmic ❑ antihypertensive ❑ anticonvulsant ❑ beta-blockers ❑ digitalis preparations ❑ diuretics ❑ ganglionic blockers ❑ others	NOTE: consider underlying condition. Potential for: exertional syncope, electrolyte imbalance, bradycardia, dysrhythmias, impaired coordination and reaction time, heat intolerance. May alter resting and exercise ECG's and exercise test performance.
Other	❑ post-exercise syncope	moderate program
	❑ heat intolerance	prolong cool-down with light activities; avoid exercise in extreme heat
	❑ temporary minor illness	postpone until recovered
	❑ cancer	if potential metastases, test by cycle ergometry, consider non-weight bearing exercises; exercise at lower end of prescriptive range (40-65% of heart rate reserve), depending on condition and recent treatment (radiation, chemotherapy); monitor hemoglobin and lymphocyte counts; add dynamic lifting exercise to strengthen muscles, using machines rather than weights.

*Refer to special publications for elaboration as required

The following companion forms are available online: www.csep.ca/publications

The **Physical Activity Readiness Questionnaire (PAR-Q)** - a questionnaire for people aged 15-69 to complete before becoming much more physically active. Please return the completed form to the participant or his/her physical activity professional.

The **Physical Activity Readiness Medical Examination for Pregnancy (PARmed-X for PREGNANCY)** - to be used by physicians with pregnant patients who wish to become more physically active. Please return the completed form to the participant or his/her physical activity professional.

For more information, please contact the:

Canadian Society for Exercise Physiology
370-18 Louisa Street
Ottawa, Ontario K1R 6Y6
Tel. 1-877-651-3755 • Online: www.csep.ca

Note to physical activity professionals...

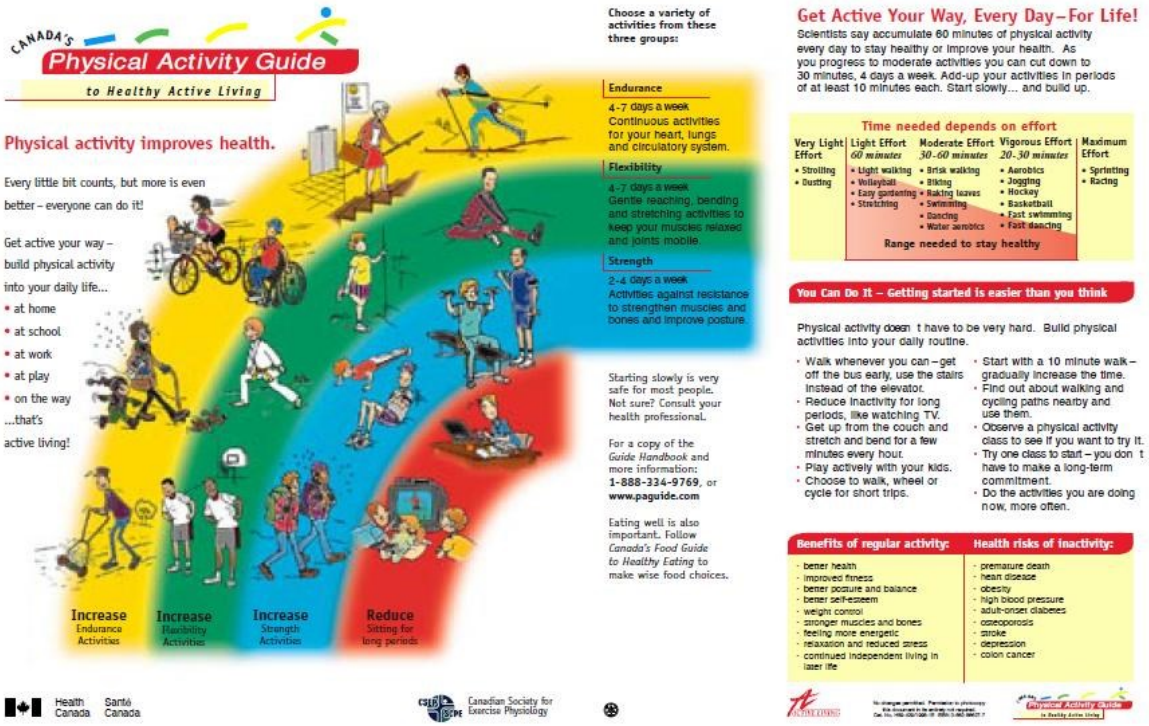
It is a prudent practice to retain the completed Physical Activity Readiness Conveyance/Referral Form in the participant's file.

Supported by: Health Canada Santé Canada

Continued on page 4...

Physical Activity Readiness
Medical Examination
(revised 2002)

PARmed-X PHYSICAL ACTIVITY READINESS MEDICAL EXAMINATION



Source: Canada's Physical Activity Guide to Healthy Active Living, Health Canada, 1998 http://www.hc-sc.gc.ca/hppb/paguide/pdf/guideEng.pdf

PARmed-X Physical Activity Readiness Conveyance/Referral Form

Based upon a current review of the health status of _____, I recommend:

- ❑ No physical activity
- ❑ Only a medically-supervised exercise program until further medical clearance
- ❑ Progressive physical activity
  - ❑ with avoidance of: _____
  - ❑ with inclusion of: _____
  - ❑ under the supervision of a CSEP Certified Exercise Physiologist®
- ❑ Unrestricted physical activity — start slowly and build up gradually

Further information:
- ❑ Attached
- ❑ To be forwarded
- ❑ Available on request

Physician/clinic stamp:

_____ M.D.

_____ 20_____
(date)

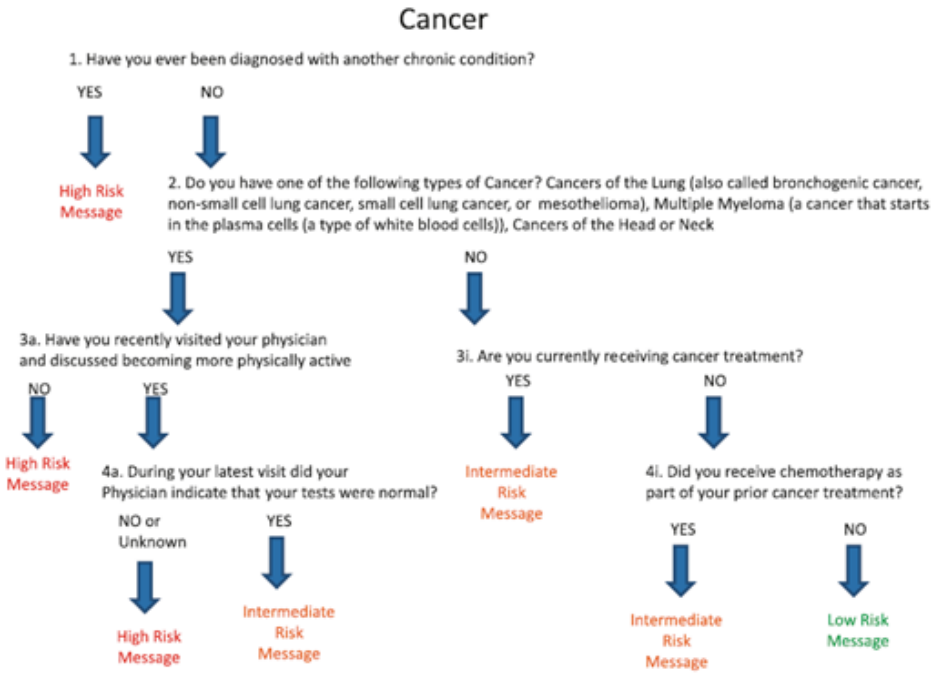
NOTE: This physical activity clearance is valid for a maximum of six months from the date it is completed and becomes invalid if your medical condition becomes worse.

4

Appendix F

Interpretation Guide of the Risk Stratification Questionnaire

Interpretation of the Risk Stratification Questionnaire



Questions 1 and 8 relate solely to participant eligibility.

Question 2 corresponds to step 1 on the above flowchart. Exceptions to the interpretation for the question will be granted to those with controlled blood pressure and controlled diabetes.

Question 3 corresponds to step 2 on the above flowchart. Persons who have had a previous diagnosis of those cancers will also be excluded in the interest of safety.

Question 4 corresponds to step 3i on the above flowchart and information about hormone treatments will be used to stratify participants during the study.

Question 5 corresponds to step 4i on the above flowchart.

Question 6 relates to participant eligibility and provides the exercise physiologist with information about medications that may necessitate modifications to the exercise program.

Question 7 corresponds to step 4a of the above flowchart.

It is assumed that by having this form completed by their physician that the participant did discuss being more physically active with their physician (see step 3a).

The Interpretation of the Risk Stratification Questionnaire will not be given to participants, and is included here to illustrate how the level of risk is determined from the questions being asked.

Appendix G

Baseline "Getting to Know You" Questionnaire

GETTING TO KNOW YOU

Thank you for taking the time to participate in this research study. The first part of the questionnaire is needed to help us learn more about you. For this reason, it is very important information. All of the information is held in strict trust and your name will **NOT** appear on any public documents. Please answer the following questions based on your **present status**.

1. How old are you? _____

2. What is the highest level of education that you have completed?

- ☐ Some high school
- ☐ Completed high school
- ☐ Some university/college
- ☐ Completed university/college
- ☐ Some technical school
- ☐ Completed technical school
- ☐ Some graduate school
- ☐ Completed graduate school

3. Marital status:

- ☐ Single/never married
- ☐ Divorced/separated
- ☐ Married/common law/living with partner
- ☐ Widowed

4. Annual income:

- ☐ less than $10,000
- ☐ $10,000-$24,999
- ☐ $25,000-$49,999
- ☐ $50,000-$74,999
- ☐ $75,000-$99,999
- ☐ $100,000-$150,000
- ☐ $150,000-$199,999
- ☐ $200,000 or more
- ☐ Do not wish to respond

Continued on Next Page

What is your current employment status? Please choose the **one** that best describes your current situation. If you are self-employed, choose full-time or part-time as appropriate.

- ☐ Working in paid job full-time (30 or more hours per week)
- ☐ Working in a paid job part-time (Less than 30 hours per week)
- ☐ Unemployed
- ☐ Unable to work because of sickness or disability
- ☐ Looking after home and/or family
- ☐ Student
- ☐ Retired
- ☐ Doing unpaid or voluntary work

6. Race/Ethnicity:

- ☐ Asian
- ☐ Black
- ☐ Caucasian
- ☐ First Nations
- ☐ Hispanic
- ☐ Other: _____

The following questions will ask you to describe your cancer diagnosis as well as details regarding the nature of your treatment and current health status.

If you have had more than one cancer diagnosis, base your answers on your ***most recent diagnosis of breast or gynecologic cancer***, please answer the following questions:

1. What type of cancer did you have? Include stage at diagnosis if possible:_____
2. In what month and year were diagnosed? _____
3. What type of treatment did you receive? (please check **ALL** that apply)

- ☐ Surgery
- ☐ Radiation therapy
- ☐ Chemotherapy
- ☐ Hormone based treatments
- ☐ Other (specify):_____

Continued on Next Page

3b. Have you completed treatment all treatments? If you are currently using a hormone treatment but have completed all other treatments check 'Yes'

☐ Yes ☐ No

3c. If you have completed treatment, when was your last treatment (month/year)? _____

4a. Have you experienced a recurrence or metastases (spread to other organs) of this cancer?

☐ Yes ☐ No

4b. Please specify (include type of recurrence, month/year of recurrence, and any treatment received):_____

_____

5a. If you have had more than one cancer diagnosis, what other type(s) of cancer did you have?

_____

5b. In what month and year was this cancer diagnosed?:

_____

5c. What type of treatment did you receive for this cancer? Please check **ALL** that apply.

☐ Surgery ☐ Radiation therapy

☐ Chemotherapy ☐ Hormone based treatments

☐ Other (specify):_____

6. Do you have any other health problems or conditions? If yes, specify.

_____

_____

7. Are you currently taking any medications? If yes, specify.

_____

_____

_____

Continued on Next Page

LEISURE TIME EXERCISE QUESTIONNAIRE

The following portion of the questionnaire will asks you to recall your *average weekly* level of physical activity *over the past month*.

When answering the following question, please remember to:

a. **Consider a typical *(average)* week over the past month.**
b. **Only count activity/exercise sessions that lasted *10 minutes or longer.***
c. **Include *all* exercise/physical activity that you do**
d. **Please also record the average duration or time that you performed each activity.**

(Please record a number in each of the spaces provided below. If you did no activity, then please record as "0")

A. STRENUOUS ACTIVITY (heart beats rapidly, sweating)
(e.g., running, jogging, hockey, soccer, squash, cross country skiing, judo, roller blading, vigorous swimming, vigorous long distance bicycling, vigorous aerobic classes, heavy weight training, laser tag)

During the past month, in an average week I was involved in *strenuous activities* _____ times/week for an average duration of _____ minutes each session.

B. MODERATE ACTIVITY (not exhausting, light perspiration)
(e.g., fast walking, baseball, tennis, easy bicycling, shooting hoops, volleyball, badminton, easy swimming, alpine skiing, popular and line dancing, leisure skating)

During the past month, in an average week I was involved in *moderate activities* _____ times/week for an average duration of _____ minutes each session.

C. MILD ACTIVITY (minimal effort, no perspiration)
(e.g., easy walking, yoga, archery, fishing, bowling, horseshoes, golf, darts, frisbee)

During the past month, in an average week I was involved in *mild activities* _____ times/week for an average duration of _____ minutes each session.

Continued on Next Page

FACT-F (Version 4)

Below is a list of statements that other people with your illness have said are important**. Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.**

	ADDITIONAL CONCERNS	**Not at all**	**A little bit**	**Some -what**	**Quite a bit**	**Very much**
H17	I feel fatigued	0	1	2	3	4
H112	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble <u>starting</u> things because I am tired	0	1	2	3	4
An4	I have trouble <u>finishing</u> things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
An16	I have to limit my social activity because I am tired	0	1	2	3	4

Continued on Next Page

The Medical Outcomes Survey Questionnaire

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.
Thank you for completing this survey!

For each of the following questions, please mark an ☒ in the one box that best describes your answer.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. <u>Compared to one year ago</u>, how would you rate your health in general <u>now</u>?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	☐ 1	☐ 2	☐ 3
b Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
c Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
d Climbing several flights of stairs	☐ 1	☐ 2	☐ 3
e Climbing one flight of stairs	☐ 1	☐ 2	☐ 3
f Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
g Walking more than a kilometre	☐ 1	☐ 2	☐ 3
h Walking several hundred metres	☐ 1	☐ 2	☐ 3
i Walking one hundred metres	☐ 1	☐ 2	☐ 3
j Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Were limited in the kind of work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d Had difficulty performing the work or other activities (for example, it took extra effort)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Did work or other activities less carefully than usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

6. **During the <u>past 4 weeks</u>, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?**

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7. **How much <u>bodily</u> pain have you had during the <u>past 4 weeks</u>?**

None	Very mild	Mild	Moderate	Severe	Very severe
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

8. **During the <u>past 4 weeks</u>, how much did <u>pain</u> interfere with your normal work (including both work outside the home and housework)?**

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

9. These questions are about how you feel and how things have been with you <u>during the past 4 weeks</u>. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the <u>past 4 weeks</u>…

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Have you been very nervous?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e. Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f. Have you felt downhearted and depressed?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g. Did you feel worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h. Have you been happy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i. Did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

10. During the <u>past 4 weeks</u>, how much of the time has your <u>physical health or emotional problems</u> interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

11. How TRUE or FALSE is <u>each</u> of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a I seem to get sick a little easier than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Thank you for completing these questions!

Appendix H

Follow-Up "Checking In" Questionnaire

Checking In

Thank you for your continued participation in this research study. This questionnaire will help us keep track of how well the strength training intervention is working. For this reason, it is very important information. All of the information is held in strict trust and your name will **NOT** appear on any public documents. Please answer the following questions based on your **present status**.

LEISURE TIME EXERCISE QUESTIONNAIRE

The following portion of the questionnaire will asks you to recall your *average weekly* level of physical activity *over the past month*.

When answering the following question, please remember to:

a. **Consider a typical *(average)* week over the past month.**
b. **Only count activity/exercise sessions that lasted *10 minutes or longer*.**
c. **Include *all* exercise/physical activity that you do**
d. **Please also record the average duration or time that you performed each activity.**

(Please record a number in each of the spaces provided below. If you did no activity, then please record as "0")

A. STRENUOUS ACTIVITY (heart beats rapidly, sweating)
(e.g., running, jogging, hockey, soccer, squash, cross country skiing, judo, roller blading, vigorous swimming, vigorous long distance bicycling, vigorous aerobic classes, heavy weight training, laser tag)

During the past month, in an average week I was involved in *strenuous activities* _____ times/week for an average duration of _____ minutes each session.

B. MODERATE ACTIVITY (not exhausting, light perspiration)
(e.g., fast walking, baseball, tennis, easy bicycling, shooting hoops, volleyball, badminton, easy swimming, alpine skiing, popular and line dancing, leisure skating)

During the past month, in an average week I was involved in *moderate activities* _____ times/week for an average duration of _____ minutes each session.

C. MILD ACTIVITY (minimal effort, no perspiration)
(e.g., easy walking, yoga, archery, fishing, bowling, horseshoes, golf, darts, frisbee)

During the past month, in an average week I was involved in *mild activities* _____ times/week for an average duration of _____ minutes each session.

Continued on Next Page

FACT-F (Version 4)

Below is a list of statements that other people with your illness have said are important**.** **Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.**

	ADDITIONAL CONCERNS	Not at all	A little bit	Some -what	Quite a bit	Very much
H17	I feel fatigued	0	1	2	3	4
H112	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble <u>starting</u> things because I am tired	0	1	2	3	4
An4	I have trouble <u>finishing</u> things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
An16	I have to limit my social activity because I am tired	0	1	2	3	4

Continued on Next Page

The Medical Outcomes Survey Questionnaire

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.
Thank you for completing this survey!

For each of the following questions, please mark an ☒ in the one box that best describes your answer.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. <u>Compared to one year ago</u>, how would you rate your health in general <u>now</u>?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a. <u>Vigorous activities</u>, such as running, lifting heavy objects, participating in strenuous sports	☐ 1	☐ 2	☐ 3
b. <u>Moderate activities</u>, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
c. Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
d. Climbing <u>several</u> flights of stairs	☐ 1	☐ 2	☐ 3
e. Climbing <u>one</u> flight of stairs	☐ 1	☐ 2	☐ 3
f. Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
g. Walking <u>more than a kilometre</u>	☐ 1	☐ 2	☐ 3
h. Walking <u>several hundred metres</u>	☐ 1	☐ 2	☐ 3
i. Walking <u>one hundred metres</u>	☐ 1	☐ 2	☐ 3
j. Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Were limited in the kind of work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d Had difficulty performing the work or other activities (for example, it took extra effort)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Did work or other activities less carefully than usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

6. **During the <u>past 4 weeks</u>, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?**

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7. **How much <u>bodily</u> pain have you had during the <u>past 4 weeks</u>?**

None	Very mild	Mild	Moderate	Severe	Very severe
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

8. **During the <u>past 4 weeks</u>, how much did <u>pain</u> interfere with your normal work (including both work outside the home and housework)?**

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

9. These questions are about how you feel and how things have been with you <u>during the past 4 weeks</u>. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the <u>past 4 weeks</u>…

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Have you been very nervous?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e. Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f. Have you felt downhearted and depressed?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g. Did you feel worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h. Have you been happy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i. Did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

10. During the <u>past 4 weeks</u>, how much of the time has your <u>physical health or emotional problems</u> interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

11. How TRUE or FALSE is <u>each</u> of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a I seem to get sick a little easier than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Thank you for completing these questions!

Thank-you for Completing This Survey!

Appendix I

Fitness Assessment Data Recording Sheet

Fitness Testing Recording Sheet **Participant ID**_____

Testing session 1 2 3 (circle one)

Bioelectric Impedance Analysis

Participant has not eaten or drank before test and meds taken at usual time □

Weight____kg Fat free mass_____ kg
Height____ cm Fat mass_____kg
Percent body fat_____%

Bench Press Predicted 1RM

Trial 1 Wt._____lbs Reps_____
Trial 2 Wt._____lbs Reps_____
Trial 3* Wt._____lbs Reps_____

1RM _____lbs $1RM = \frac{Wt.}{\%1RM}$

Leg Press Predicted 1RM

Trial 1 Wt._____lbs Reps_____
Trial 2 Wt._____lbs Reps_____
Trial 3* Wt._____lbs Reps_____

1RM _____lbs $1RM = \frac{Wt.}{\%1RM}$

*Do not Exceed more than three trials
**Most accurate results between 7 and 10 reps.

Reps	%1RM
1	100
2	95
3	92.5
4	90
5	87.5
6	85
7	82.5
8	80
9	77.5
10	75
11	72.5
12	70
13	67.5
14	65

Standard Load Test

Use a weight corresponding to 50% 1RM from their BASELINE measurement

Bench Press
Baseline 1RM_____lbs 50% Baseline 1RM_____ # of Reps_____

Leg Press
Baseline 1RM_____lbs 50% Baseline 1RM_____ # of Reps_____

Appendix J

Training Booklet

STRENGTH TRAINING PROGRAM

for

BREAST AND GYNECOLOGIC CANCER SURVIVORS

DALHOUSIE UNIVERSITY
Inspiring Minds

Capital Health

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INTRODUCTION

Thank you for choosing to participate in the *'Exercise Frequency in Breast and Gynecologic Cancer Survivors'* study. Included in this booklet is a detailed explanation of your strength training program. The following selections will help you to follow the study's strength training intervention by explaining how to choose the right sized weight, how many sets and repetitions of each exercise you should do, and how to progress though the program. There are also detailed explanations of the exercises included in the program and a recording sheet. You can refer to this manual as often as you like and are encouraged to use it.

HOW MANY REPETIONS AND SETS SHOULD I DO?

A repetition is the number of times you do a certain movement. For example, if someone was asked to do ten repetitions of a strength exercise they would need to lift AND lower the weight ten times. Groups of repetitions are referred to as a set. In the above example, the person was being asked to do one set of ten repetitions. As you progress through this strength training program the number of sets of 10-14 reps we are asking you to do will change. These changes are outlined below:

Week 1 – Introduction to Strength Training
One Set of 10 to 14 Repetitions

Weeks 2 Though 7 – Strength Training Foundation/Introductory Program
Two Sets of 10 to 14 Repetitions

Weeks 8 Through 13 – Beginner`s Strength Training Program
Three Sets of 10 to 14 Repetitions

Some exercises in this program, such as the front and side planks, are ISOMETRIC or "posture" exercises and do not involve any movement. For these exercises, it is not possible to prescribe a number of repetitions. Instead, we would like you to do these exercises by timing how long you can hold the isometric pose for and doing the required number of sets. For example, on week five Mary did two sets of front plank, she could do the first set for 27 seconds and the second set for 23 seconds.

HOW MUCH WEIGHT SHOULD I LIFT?

The amount of weight you should lift depends on how many repetitions of a given exercise you are doing. The goal of choosing an appropriate sized weight in this study is to select a weight that will allow you to do **at least** 10 repetitions in good form and no more than 14 on every set. For example, on week ten Betty is able to 15 repetitions of chest press with a 30lb weight for all three of her sets, the next day she exercises she should try lifting 35lbs. Another example would be Linda who can't do ten repetitions of leg press with 50lbs; she should try a smaller weight.

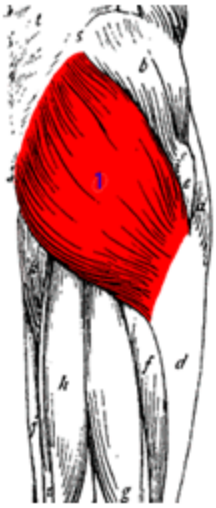
REMEMBER, SAFTEY FIRST!!!

As a general rule, if you are unfamiliar with an exercise try a smaller weight first. All exercise sessions will be supervised and you are encouraged to ask as many questions as you need, especially when doing an exercise for the first time. Also, if you are planning on lifting more weight because you can do more than 14 repetitions check with the exercise physiologist (Tim Gravelle) or the fitness instructor first, and please do not add more than 5lbs at a time.

LIST OF EXERCISES

For each muscle group there are at least two exercises listed a Standard Exercise and one or more Modified Exercises. Unless you have a functional disability (such as lymphedema) **AND** the permission of the exercise physiologist you are being asked to do the Standard Exercise.

Muscle Group: Legs and Buttocks



Standard Exercise: Leg Press

A. Sit on machine with back on padded support. Place feet slightly high on platform, so that your knees do not go past your toes. Extend hips and knees. Release safety lever and grasp handles to sides.

B. Flex hips and knees to lower the weight until hips are completely flexed. Push platform by extending knees and hips. Repeat.

A 

B 

Modified Exercise: Forward Lunge

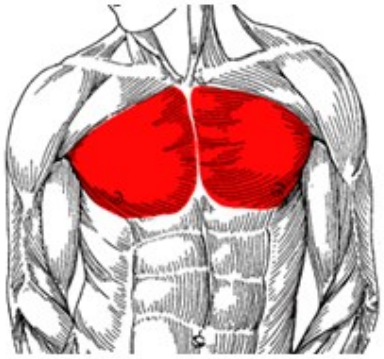
A. Stand with hands on hips or clasped behind neck. You may wish to hold dumbbells to increase the difficulty of this exercise.

B. Lunge forward with the first leg. Land on heel then forefoot. Lower body by flexing knee and hip of front leg until knee of rear leg is almost in contact with floor. Return to original standing position by forcibly extending hip and knee of forward leg. Repeat by alternating lunge with opposite leg.

A 

B 

Muscle Group: Chest



Primary Exercise: Chest Press

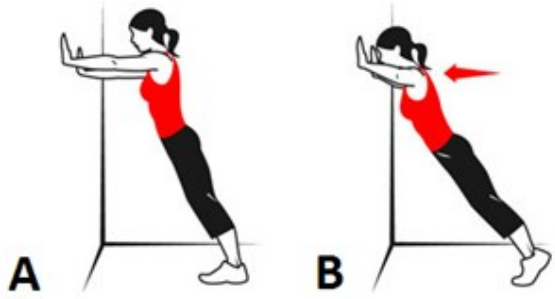
A. Sit on seat with upper chest just above handles. Grasp handles with wide overhand grip; elbows out to sides just below shoulders.

B. Push forward until arms are extended. Return weight until chest muscles are slightly stretched. Repeat.

Modified Exercise: Wall-Push Up

A. Stand next to a wall so that you need to lean forward slightly to touch the wall with fully extended arms.

B. Bend your elbows so that your nose nearly touches the wall then push against the wall until you return to the beginning position. Repeat.



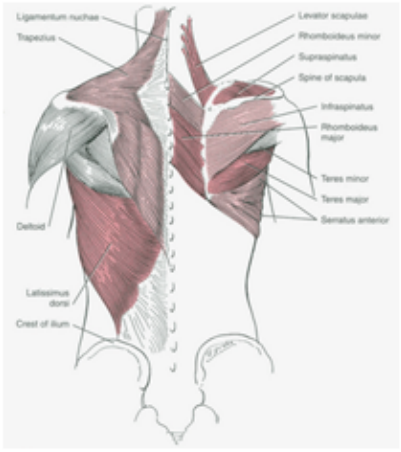
Modified Exercise: Punch Forward

A. In a standing position, hold the elastic tubing so that it goes around your back and both ends are being held close to your body and the band it taught.

B. Extend your arms until they are straight. Repeat.

Muscle Group: Upper Back

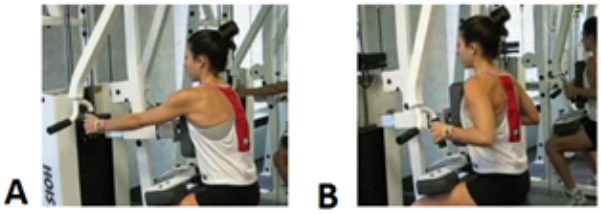
Standard Exercise: Seated Row



A. Sit on seat and position chest against pad. Grasp lever handles with underhand grip.

B. Pull the handles back until elbows are behind back and shoulders are pulled back. Return until arms are extended and shoulders are stretched forward. Repeat.

This exercise can also be done with a cable machine



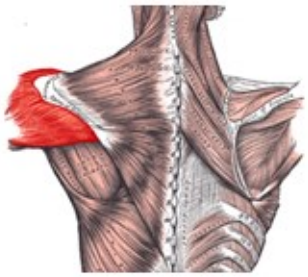
Modified Exercise: Scapular Squeezes

Sit on an armless chair or stool. Keeping your chin tucked in and your chest high, pull your shoulder blades together. Hold for five seconds, and then relax. Repeat.

This exercise can be done with a partner to increase the resistance. Have your partner gently push back against your shoulder blades so that you are able to complete 10-14 repetitions


Scapular squeezes

Muscle Group: Shoulders



Standard Exercise: Shoulder Press

A. Grasp lever handles to each side with overhand grip.

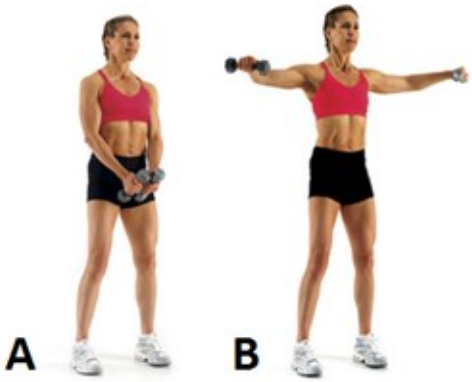
B. Press lever upward until arms are extended overhead. Lower and repeat.

Modified Exercise: Lateral or Front Shoulder Raises

A. Grasp dumbbells in both hands. Position dumbbells in front of upper legs for a front raise (left), or in front of your pelvis with the palms together lateral raise (right). Elbows should be straight or slightly bent.

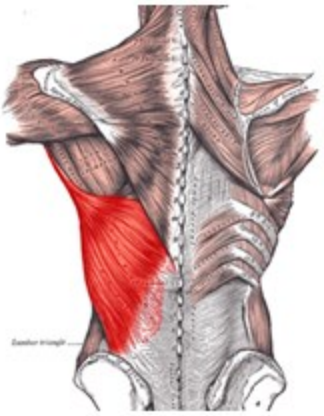
B. Raise dumbbells upward until upper arms are at or above horizontal. For a front raise the dumbbells should stay in front of your body. For a side raise the dumbbells should stay to your side. Lower and repeat.

Front Raise



Lateral Raise

Muscle Group: Middle Back (Lats)



Standard Exercise: Lat. Pull

A. Sit on seat. Reach up and grasp handles with wide overhand grip.

B. Pull levers down to sides of shoulders. Return until arms and shoulders are fully extended. Repeat.

A 

B 

Modified Exercise: Close-Grip Pull Down

A. Grasp lever bars directly above shoulders using a close grip. Sit with thighs under supports.

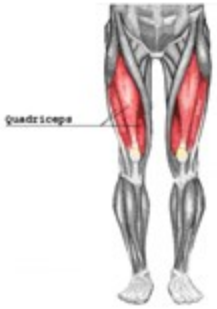
B. Pull down cable attachment or bar to chest. Return until arms and shoulders are fully extended. Repeat.

A 

B 

Muscle Group: Quadriceps

Standard Exercise: Leg Extension



A. Sit on seat with back against padded back support. Place front of lower legs under padded lever above your shoes. Adjust the seat so that your knee is in line with the machine's axis of rotation. Grasp handles on the sides for support.

B. Move lever forward and upward by extending knees until the legs are straight. Return lever to original position by bending knees. Repeat.

A   B

Modified Exercise: Standing Leg Extension

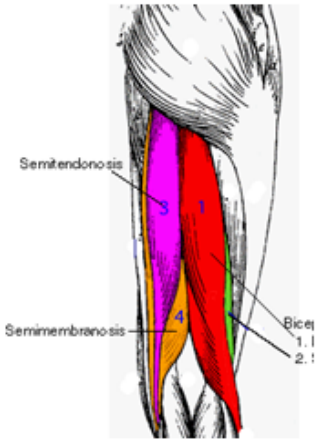
A. Stand facing away from low pulley or thera-band securely attached to a low anchor. Secure the foot in the cable attachment or loop the thera-band around the ankle. Hold onto a nearby wall, partner or other prop for support. Stand forward on free leg. Raise knee up positioning thigh approximately 45° forward. Allow lower leg attached to cable to be pulled back.

B. Keeping the thigh stationary, extend lower leg forward until leg is straight. Return by lowering lower leg down and back to original position. Repeat. Alternate legs.

A 

B

Muscle Group: Hamstrings



Standard Exercise: Ham Curl

A. Sit on machine with back against padded back support. Place back of lower leg on top of padded lever. Secure lap pad against thigh just above knees. Grasp handles on lap support.

B. Pull lever to back of thighs by flexing knees. Return lever until knees are straight. Repeat.

A

B

B

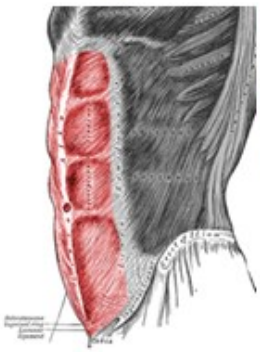
Modified Exercise: Standing Ham Curl

A. Loop a resistance band around one ankle and step on the other end of the band, leave enough tension so that the band is tight when feet are about a foot apart. Stand in front of a wall or other support and hold onto it for balance if you need to.

B. Bend the leg with the resistance band around it until your knee is at 90°.

You can also use ankle weights instead of a resistance band.

Muscle Group: Abdominals



Standard Exercise: Front Plank (ISOMETRIC)

Lie prone on mat. Place forearms on mat, elbows under shoulders. Place legs together with forefeet on floor. Raise body upward by straightening body in straight line. Hold position as long as possible.

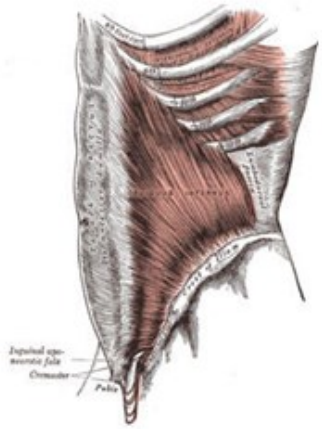
Modified Exercise: Front Plank on Knees (ISOMETRIC)

Lie prone on mat. Place forearms on mat, elbows under shoulders. Place legs together with knees on floor. Raise body upward by straightening body in straight line. Hold position as long as possible.

Muscle Group: Obliques

Standard Exercise: Side Plank (ISOMETRIC)

Lie on side on mat. Place forearm on mat under shoulder perpendicular to body. Place upper leg directly on top of lower leg and straighten knees and hips.
Raise body upward by straightening waist so body is ridged. Hold position as long as possible then repeat with opposite side.



Modified Exercise: Side Plank on Knees (ISOMETRIC)
Lie on side on mat. Place forearm on mat under shoulder perpendicular to body. Bend knees at a right angle. Place upper leg directly on top of lower leg and straighten hips. Raise body upward by straightening waist so hips and waist are ridged. Hold position as long as possible and repeat with opposite side.

WHAT IF I GET HURT OR BECOME SICK?

Despite our best efforts you may become hurt or sick during this study, either inside or outside of the study. If this happens, it is your responsibility to report it to a member of the research team. Doing so helps ensure your safety and provides the researchers with valuable information about the safety of strength training. Please report all illnesses and injuries to the research team including those that occur outside of the study.

STRENGTH TRAINING RECORDING SHEET

		Week 1	Week 2		Week 3		Week 4		Week 5		Week 6		Week 7		Week 8			Week 9			Week 10			Week 11			Week 12			Week 13		
Muscle Group	Set	1	1	2	1	2	1	2	1	2	1	2	1	2	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
Buttocks	Day 1																															
	Day 2																															
Chest	Day 1																															
	Day 2																															
Upper Back	Day 1																															
	Day 2																															
Shoulders	Day 1																															
	Day 2																															
Middle Back	Day 1																															
	Day 2																															
Quadriceps	Day 1																															
	Day 2																															
Hamstrings	Day 1																															
	Day 2																															
Abdominals	Day 1																															
	Day 2																															
Obliques	Day 1																															
	Day 2																															
Example	Day 1	10	12	12	14	13	14	14	15	15	10	10	12	11	13	12	12	12	14	13	12	14	14	13	15	15	15	10	10	10	11	11
"Ham Curl"	Day 2	12	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Note that in the example provided the name of the exercise you will be doing needs to be filled in underneath the name of the muscle group. This is an example for someone in the once-a-week group, if you are in the twice-a-week group fill in both day 1 and 2.

Week 1 – Introduction to Strength Training
One Set of 10 to 14 Repetitions
Weeks 2 Though 7 – Strength Training Foundation Program
Two Sets of 10 to 14 Repetitions
Weeks 8 Through 13 – Beginner`s Strength Training Program
Three Sets of 10 to 14 Repetitions

APPENDIX K

Supplementary Tables

Table S1. Changes in muscular fitness outcomes.

Measure	Group	Baseline	Week 7	Week 13		Repeated Measures ANOVA			
		M(Range)	M (Range)	M (Range)	Analysis	η2	Power	*p*	Est. Sample
Leg Press 1RM (kg)	1d/wk	117.3 (84.4-175.3)	123.2 (99.7-147.1)	132.0 (99.7-191.6)	Within	0.72	0.92	0.01**	6
	2d/wk	128.6 (104.9-181.8)	153.0 (104.9-230.8)	159.1 (104.9-227.3)	Between	0.11	0.16	0.324	436
Bench Press 1RM (kg)	1d/wk	23.7 (19.5-27.8)	25.0 (20.1-31.1)	25.9 (20.2-35.2)	Within	0.57	0.67	0.03*	6
	2d/wk	27.5 (13-36.4)	31.6 (23.6-39.0)	33.6 (23.6-42.2)	Between	0.27	0.36	0.11	74
Leg Press SLT (reps)[a]	1d/wk	34.6 (24-41)	44.4 (24-62)	53.0 (25-88)	Within	0.52	0.57	0.05	8
	2d/wk	35.9 (24-45)	45.3 (40-50)	52.7 (44-74)	Between	0.00	0.05	0.93	2096
Bench Press SLT (reps)	1d/wk	28.6 (17-39)	37.4 (20-50)	39.0 (26-50)	Within	0.87	1	0.00***	4
	2d/wk	26.5 (13-44)	33.8 (24-47)	36.7 (24-57)	Between	0.02	0.068	0.67	1456

Note: Estimated sample size uses assumes an 80% power to detect a significant difference at α = 0.05. η2 = Partial eta Squared. 1RM = One repetition maximum. SLT = Standard load test. 1d/wk = Once-a-week group. 2d/wk = Twice-a-week group. Est. Sample = Estimated Sample Size.

[a] Pillai's trace.

*p< 0.05. **p<0.01. ***p<0.001

Table S2. Changes in body composition outcomes.

Measure	Group	Baseline M (Range)	Week 7 M (Range)	Week 13 M (Range)	Repeated Measures ANOVA Analysis	η2	Power	*p*	Est. Sample
Weight (kg)	1d/wk	69.3 (49.3-85.6)	69.9 (52.1-85.8)	69.4 (52.1-86.7)	Within	0.39	0.37	0.14	12
	2d/wk	73.8 (59.5-91.8)	73.8 (59.5-91.4)	73.5 (59.5-91.1)	Between	0.03	0.08	0.60	5816
Lean Body Mass (kg)[a]	1d/wk	43.4 (39.0-49.9)	43.4 (39.6-49.6)	43.0 (38.8-50.3)	Within	0.09	0.09	0.70	3217094
	2d/wk	45.9 (41.8-49.3)	42.6 (26.0-49.4)	46.0 (41.1-50.2)	Between	0.04	0.08	0.57	3294
Body Fat (%)	1d/wk	33.5 (20.5-42.5)	36.7 (22.6-42.5)	36.8 (22.6-43.7)	Within	0.21	0.17	0.39	34
	2d/wk	37.2 (28.9-46.3)	36.9 (28.9-46.0)	36.8 (28.9-44.9)	Between	0.01	0.06	0.78	52328

Note: Estimated sample size uses assumes an 80% power to detect a significant difference at α = 0.05. η2 = Partial eta Squared. 1d/wk = Once-a-week group. 2d/wk = Twice-a-week group. Est. Sample = Estimated Sample Size.

[a] Pillai's trace.

Table S3. Changes in quality of life and fatigue outcomes.

Measure	Group	Baseline	Week 7	Week 13	Repeated Measures ANOVA				
		M (Range)	M (Range)	M (Range)	Analysis	η2	Power	*p*	Est. Sample
Physical Funct.	1d/wk	76.4 (7-100)	74.4 (7-100)	74.4 (7-100)	Within	0.35	0.32	0.16	14
	2d/wk	69.2 (40-95)	81.7 (70-100)	80.0 (65-100)	Between	0.00	0.05	0.92	523274
Role Physical	1d/wk	65.0 (6.25-100)	76.3 (6.3-100)	63.8 (6.3-100)	Within	0.24	0.2	0.33	26
	2d/wk	60.4 (12.5-100)	67.7 (12.5-100)	64.6 (12.6-100)	Between	0.00	0.05	0.86	523274
Bodily Pain[a]	1d/wk	80.6 (61-100)	68.8 (62-84)	77.4 (51-100)	Within	0.22	0.19	0.36	30
	2d/wk	55.5 (22-84)	55.7 (22-84)	59.2 (22-84)	Between	0.21	0.28	0.16	122
General Health	1d/wk	61.2 (35-97)	69.6 (35-92)	63.8 (30-95)	Within	0.20	0.17	0.40	36
	2d/wk	44.7 (0-72)	50.5 (0-97)	45.5 (0-87)	Between	0.09	0.13	0.37	646
Vitality	1d/wk	57.5 (12.5-87.5)	60.0 (12.5-81.3)	52.5 (12.6-87.5)	Within	0.10	0.10	0.66	138
	2d/wk	49.0 (0-75)	53.1 (0-75)	50.0 (0-81.3)	Between	0.01	0.06	0.75	523274
Social Funct.	1d/wk	72.5 (25-100)	80.0 (25-100)	75.0 (25-100)	Within	0.39	0.37	0.14	12
	2d/wk	60.4 (0-100)	79.2 (0-100)	62.5 (0-100)	Between	0.02	0.07	0.70	13084

Role Emotion	1d/wk	68.3 (8.3-100)	81.7 (8.3-100)	76.7 (8.3-100)	Within	0.28	0.24	0.26	20
	2d/wk	69.4 (0-100)	73.6 (0-100)	73.6 (0-100)	Between	0.00	0.05	0.89	523274
Mental Health	1d/wk	51.0 (15-95)	67.0 (15-85)	68.0 (15-95)	Within	0.23	0.19	0.35	28
	2d/wk	60.8 (0-90)	66.7 (0-90)	62.5 (0-95)	Between	0.00	0.05	0.95	523274
PCS	1d/wk	52.2 (36.8-65.5)	50.9 (45.3-58)	49.8 (30.1-64.1)	Within	0.02	0.06	0.92	36
	2d/wk	42.5 (32.5-51.5)	45.3 (30-52)	45.0 (31.1-56.3)	Between	0.16	0.21	0.23	208
MCS	1d/wk	40.8 (10.4-57.1)	46.4 (10.4-57.6)	44.5 (10.4-59.5)	Within	0.22	0.18	0.37	30
	2d/wk	41.9 (1.3-62.8)	45.4 (1.3-59)	42.1 (1.3-58.3)	Between	0.00	0.05	0.95	523274
Fatigue	1d/wk	40.6 (15-51)	32.6 (15-47)	36.8 (15-51)	Within	0.10	0.10	0.64	138
	2d/wk	30.6 (10-48)	34.5 (10-47)	32.7 (10-50)	Between	0.02	0.07	0.68	13084

Note: Estimated sample size uses assumes an 80% power to detect a significant difference at $\alpha = 0.05$. Higher scores represent better quality of life and lower fatigue. $\eta 2$ = Partial eta Squared. Funct. = Functioning; PCS = Physical Composite Score. MCS = Mental Composite Score. 1d/wk = Once-a-week group. 2d/wk = Twice-a-week group. Est. Sample = Estimated Sample Size.

[a] Pillai's trace.

APPENDIX L

Analysis of Baseline Physical Activity

Despite being non-significant and experimental groups being stratified on meeting physical activity guidelines to accumulate 150 minutes of moderate-vigorous physical activity (MVPA) there was a considerable difference in mean MVPA noted at baseline. It is possible that if this trend were to continue as more participants were added to the study than a significant confound would exist. Below re-prints the MVPA data at baseline, the independent samples t-test, estimates Cohen's d effect size, power, and estimates a sample size where this difference may become significant.

Table S4. Baseline physical activity data.

Measure	Overall (n = 11)	1 day/week (n = 5)	2 days/week (n = 6)	*p*
MVPA (min/week)	121.8(201.2)	64.0(89.6)	170(261.6)	0.41

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
BL_PA_Mod_Vig	Equal variances assumed	1.574	.241	-.858	9	.413	-106.00000	123.49119	-385.35648	173.35648
	Equal variances not assumed			-.929	6.350	.387	-106.00000	114.07308	-381.44220	169.44220

Figure S1. Independent samples t-test of baseline physical activity data.

Cohen's d = M1 - M2 / σ pooled
where σ pooled =√[(s 12+ s 22) / 2]

Cohen's d effect size = -0.54

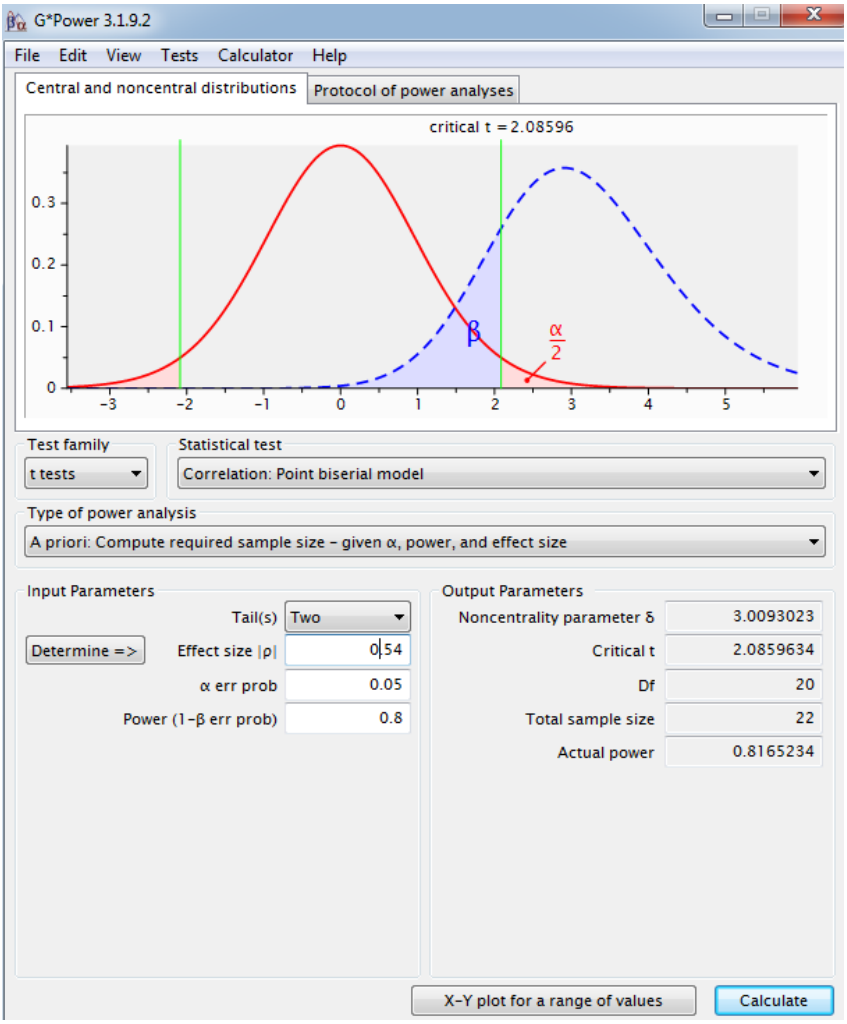


Figure S2. GPower sample size and power calculator estimation of baseline MVPA data.

Observed power = 0.82
Sample Size n = 22