Feasibility of Implementing Personalized Exercise for Prostate Cancer Survivors

by

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ABSTRACT

Introduction: Prostate cancer is the most common cancer among Canadian men. Exercise has been shown to increase physical function, decrease the risk of recurrence, and improve the quality of life of men with prostate cancer. Aerobic and resistance exercise are seen as beneficial for this population; however, research has primarily examined general exercise protocols, with prescriptions generally following public health guidelines for physical activity. Personalized exercise programs may prove beneficial to men with prostate cancer to support their specific needs following cancer treatment.

Objectives: To examine the feasibility of implementing a personalized exercise program for men with prostate cancer.

Methods: A single-arm before and after trial including men with prostate cancer. Two weekly exercise training sessions were conducted including one group personal training session and one group circuit training class over the 12-week period. Feasibility was assessed at the level of the exercise specialist; examining time requirements, expertise levels, and equipment needs. Feasibility was measured at the level of the participant by evaluating need for exercise modifications, program adherence and physical fitness outcomes.

Results: Twenty-four participants with a mean age of 67.7 years participated in the study. The primary identified barriers to exercise were fatigue, existing co-morbid health and musculoskeletal conditions, and incontinence. Sixteen participants (67%) required modifications to standard exercise programming with five participants requiring physiotherapy consult, three requiring concurrent physiotherapy treatment, and two requiring specialist care to address incontinence. The cost of the additional interdisciplinary services over standard exercise programming was estimated

at $3643.43. Significant improvements were found in upper and lower body strength, six-minute walk distance, number of sit-to-stands, and waist circumference.

Conclusions: Among participants, cancer-related fatigue and existing musculoskeletal/ co-morbid conditions were reported as primary barriers to exercise participation. Closer attention to the monitoring and reporting of adherence to exercise prescription variables of intensity, frequency, and duration may better inform the dosage of exercise needed to obtain fitness benefits. Our findings suggest that many prostate cancer survivors, especially those with other health and musculoskeletal issues, may benefit from an interdisciplinary team approach to personalize exercise. Further research is needed to further evaluate the cost benefit of this approach.

PREFACE

This thesis is an original work by Kaitlyn Boudreau and Co-Authored by Dr. Margaret L. McNeely, Dr. Brita Danielson, and Dr. Kerry Courneya. This research study received ethical approval from the Health Research Ethics Board of Alberta: Cancer Committee under the parent study “Alberta Cancer Exercise (ACE)”.

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DEFINITIONS AND ABBREVIATIONS

1. **Prostate cancer:** The abnormal, uncontrolled growth of mutated cells in the prostate gland that can form a malignant tumor. Prostate cancer can spread (metastasize) to other parts of the body. Prostate cancer is the most common cancer among Canadian men.
2. **Exercise specialist:** A kinesiologist, certified exercise physiologist, or other exercise expert with post-secondary education in the field of exercise science.
3. **CSEP-CEP:** An exercise physiologist with a designation from the Canadian Society of Exercise Physiology. Scope of practice includes fitness assessments, prescription, and supervision for both healthy and chronic disease populations.
4. **Proctitis:** Inflammation of the lining of the rectum
5. **Dysuria:** Painful urination
6. **Hematuria:** Blood in urine
7. **Intervention:**

   4.1: Single-arm trial: A study in which all approved participants are enrolled and receive the treatment or intervention.

   4.2: Feasibility: The state in which something can be easily or conveniently done.

   4.3: Preliminary efficacy: examination of data to determine treatment effect (trends), even if underpowered to detect significant differences.

   4.4: ACE: Alberta Cancer Exercise

   4.5: 6MWT: The 6-minute Walk Test used to assess individual's ability to cover as much walking distance as possible in six minutes.

   4.6: STS: Sit-to-Stand test is an assessment tool used to test lower extremity strength and function.

   4.7: UPST: Uni-pedal stance test is used to assess standing balance an assessment on one leg at a time.

   4.8: 1-RM: One-repetition maximum test is the maximal amount of weight an individual can push, pull or lift only one time.

5. Outcomes:

   5.1: Workload: prescription of exercise variables of intensity, repetitions and sets.

5.2: Functional capacity: A set of tests used to determine the functional ability of an individual to perform activities of daily living.

5.3: Anthropometric measures: Physical body composition of the human body estimated by height, weight and measures of waist and hip circumference.

CHAPTER 1: INTRODUCTION

1.1 Review of prostate cancer

Prostate cancer accounts for 23.4% of all cancer cases among males and 9.5% of cancer related deaths in men (Ellison, 2016). It is estimated that in 2017, there were 21,300 new cases of prostate cancer with 66 men being diagnosed every day (Smith et al., 2018). There has been a 3.8% decline in the rate of newly diagnosed cases of prostate cancer, believed to be due to changes to screening practices (Ellison, 2016). Furthermore, in Canada when all cancers are combined, prostate cancer has the third highest five-year survival rate at 95% (Canadian Cancer Society, 2016).

Prostate cancer is often considered a long-term condition, as men are living longer; however, these men often suffer with long-term effects from treatment that require interdisciplinary support and strategies to improve well-being. Prostate cancer has a high disease burden in terms of its negative impact on quality of life; therefore, it is important to identify affordable and realistic strategies to improve the lives of these men (Friedenreich et al., 2016).

1.1.1 Exercise and prostate cancer

Exercise has been established as an effective method to address the adverse side effects following prostate cancer treatment. Studies including systematic reviews, cohort studies, and meta-analyses have examined the effects of exercise in conjunction with current treatment options, and have shown positive changes in quality of life, fatigue, body composition, and exercise behaviors. In 2016, a systematic review and meta-analysis on exercise for men with prostate cancer examined 16 randomized control trials involving over 1500 men with prostate cancer (Bourke et al., 2016). Results supported the benefit of exercise interventions to improve cancer specific quality of life, fatigue, lower body strength, and aerobic fitness. Moreover, borderline positive effects were found for sexual activity (Bourke et al., 2016). The key recommendations from the review included further research to evaluate: (1) exercise programs that are tailored to the individual's capabilities and limitations; (2) behavior change interventions to optimize adherence to exercise; and (3) the cost-effectiveness of exercise to inform integration into healthcare services (Bourke et al., 2016).

1.2 Statement of the problem

According to Statistics Canada, prostate cancer is the most common cancer and is the third leading cause of cancer death among Canadian men (Canadian Cancer Society, 2016). There are several effective treatment options for the management of prostate cancer (Heidenreich et al., 2014); however, despite advancements, cancer treatments still negatively impact quality of life, and increase the risk of developing or worsening existing co-morbid conditions. Exercise is increasingly recognized, in conjunction with other medical and supportive care treatment options, as a management tool to help reduce the adverse side effects caused by cancer treatment through reducing cancer-specific fatigue, increasing exercise capacity and muscular strength, and improving quality of life (Bourke et al., 2015). To date, little is known about the appropriate amount and duration of exercise that is most beneficial, and if there are any long-term benefits from participating in regular exercise for men living with prostate cancer. Furthermore, it is unknown what delivery method is the most beneficial for men, and to what extent exercise programs are feasible with current clinical resources and expertise.

1.3 Research Questions

1. To what extent is a personalized exercise program acceptable, appropriate, and beneficial to program recipients?
2. To what extent can a personalized exercise program be successfully delivered to intended participants in some defined, but not fully controlled, context?
3. To what extent can a personalized exercise program be carried out with intended participants within the context of existing clinical resources and expertise?

1.4 Hypothesis

1.4.1 Hypothesis related to Feasibility:

1. We hypothesized that the participants would attend and adhere to >80% of the prescribed exercise sessions.
2. We hypothesized that the time to plan and conduct a personalized exercise intervention would not exceed 12 hours a week.
3. We hypothesized that a personalized exercise program would address barriers to exercise.

1.4.2 Hypothesis related to Study Outcomes:

1. We hypothesized that a personalized exercise program would show trends towards better functional capacity, muscular strength, and anthropometric measures.

1.5 Limitations

This feasibility study had multiple limitations due to the design. Namely, the small sample size, limiting the ability to detect differences in outcomes. Furthermore, the study was designed as a single-arm before and after trial and lacked a control group for comparison. The men participating in the study had previously been participants in the TrueNTH lifestyle management program, a group-based, generalized physical exercise program for men with prostate cancer. The men had exercised at the Cancer Rehabilitation Clinic at the University of Alberta for at least one 12-week session in the previous year.

1.6 Ethical considerations

Ethical approval was obtained from the Health Research Ethics Board of Alberta: Cancer Committee, as a sub-study of the "Alberta Cancer Exercise Hybrid Effectiveness-Implementation Study". Participants were asked to sign a consent form outlining confidentiality, all potential risks and benefits, and the right to withdraw (See Appendix A). Participants were free to withdraw from the study at any time. All identifying information, including personal and medical information were entered into the secure REDCap database supported by the Women and Children's Health Research Institute, housed in the Faculty of Medicine and Dentistry at the University of Alberta. All other documents related to the exercise prescription were coded by study ID and initials, and retained in a locked filing cabinet at the Cancer Rehabilitation Clinic.

CHAPTER 2: LITERATURE REVIEW

Men diagnosed with prostate cancer may be offered a number of different cancer treatment options. The most commonly prescribed treatments are active surveillance, surgery, radiation therapy, and hormone therapy (Harvard Medical School, 2016). While these treatments aim to cure, control or monitor the cancer, many are associated with side effects. Physical side effects are common and may include sexual dysfunction (Higano, 2012), urinary incontinence (Resnick et al., 2013), reduced muscle strength, reduced bone and lean mass, and increased fat mass (Galvão et al., 2008; Ahmadi & Daneshmand, 2014). Psychological side effects may include fatigue (Pachman, Barton, Swetz, & Loprinzi, 2012), depression and anxiety (Watts et al., 2014), and decreased quality of life (Miller et al., 2018). Exercise, in conjunction with treatment, is now recognized as an effective lifestyle management strategy to improve physical and psychological well-being for men living with prostate cancer (Schmitz et al., 2010).

Active surveillance / Watchful waiting

Active surveillance is an option when the individual has low-risk, slow-growing or favourable-risk prostate cancer (Tosoian et al., 2015). Studies have shown that exposing these men to prostate cancer treatment, when the clinical benefit for the cancer is minimal, may lead to side effects negatively impacting function and quality of life (Davison, Breckon, & Hons, 2012). A cohort study examining nearly 1,300 men, on active surveillance for 19 years, showed that the prostate cancer specific survival rate was 99% at the 15-year follow-up, with around half of the men needing cancer treatment at a median of 8.5 years from diagnosis (Tosoian et al., 2015).

Watchful waiting or observation is different from active surveillance. Watchful waiting is an option when there is no viable treatment plan for the prostate cancer, due to either the individual's age or health status (Harvard Medical School, 2016). While no physical side effects of the cancer treatment may need to be considered with surveillance and watchful waiting, exercise specialists working with these survivors should be aware of the need for ongoing surveillance of symptoms such as reports of new bone pain.

Radical local treatment / Radical prostatectomy

A radical prostatectomy is the surgical removal of the entire prostate gland, the seminal vesicles, and may include lymphadenectomy in the pelvic region (Harvard Medical School, 2016). Indications for performing a radical prostatectomy include a Gleason score between 6-7,

Prostate-specific antigen (PSA) level < 20, and a life expectancy of > 10 years (Heidenreich et al., 2014). Radical prostatectomy has been shown to have a cancer-specific survival benefit when compared to watchful waiting; however, side effects such as urinary incontinence can greatly impact the survivor's quality of life (Holmberg et al., 2012).

Urinary incontinence is defined as any involuntary leakage of urine (Abrams et al., 2003). When compared to community-dwelling men, urinary bother and incontinence was substantially higher in men with prostate cancer. Furthermore, incontinence issues were found to increase with survivorship duration (Kopp et al., 2013). Urinary incontinence may be a barrier to exercise for men with prostate cancer due to the repeated need to go to the bathroom, embarrassment of leakage, and the inability to control bladder leakage while completing exercises (Er et al., 2017).

There are therapeutic approaches that can be used to counteract the incontinence issues such as pelvic floor exercises, biofeedback, and electrical stimulation. At present, the evidence is conflicting on the efficacy of these treatments; however, early initiation of physiotherapy has been shown to improve symptoms and result in earlier resolution of incontinence (Rajkowska-Labon, Bakuła, Kucharzewski, & Śliwiński, 2014). Specifically, research has shown that both preoperative and post-operative exercises led by a physiotherapist may significantly lower incontinency rates in survivors one to three months post-surgery when compared to post-operative alone (Centemero et al., 2010). Moreover, when pelvic floor muscle training is provided by a health care professional such as a physiotherapist, an improvement in continence rates over time is generally observed (Overgård, Angelsen, Lydersen, & Mørkved, 2008).

Radiation

Radiation therapy is a common treatment for a variety of cancers, including prostate cancer. Radiation can be delivered through external beam radiation or brachytherapy – the surgical implantation of small radioactive pellets into the prostate gland (Harvard Medical School, 2016). Radiation therapy is considered a reasonable alternative to surgery for early-stage prostate cancer, and may be used in conjunction with other therapies depending on the stage of the cancer, and the risk profile of the patient (Harvard Medical School, 2016). The most common complaints of men receiving radiation therapy include: bladder and bowel dysfunction, erectile dysfunction, and fatigue (Harvard Medical School, 2016). Cancer-related-fatigue is the most common reported treatment-related side effect in men with prostate cancer (Baguley, Bolam, Wright, & Skinner, 2017). Exercise is recognized as a strategy that can reduce fatigue

and improve quality of life (Taaffe et al., 2017). Specifically, aerobic and resistance training have been shown to mitigate fatigue in men receiving radiotherapy, with resistance training resulting in better long-term benefit (Segal et al., 2009). While exercise can be beneficial, it is important to modify exercise programs if men are experiencing side effects such as diarrhea, dysuria, rectal bleeding, or skin reaction. Pressure and repetitive movement of the lower body/pelvic region can increase irritation to the region in early stages of the healing process.

Brachytherapy involves the implantation of 50-150 radioactive pellets near the tumor site. The pellets may be permanent or temporary and can be used as the initial therapy for early-stage patients or to boost the primary therapy in locally advanced cases (Keyes et al., 2013). Permanent brachytherapy is more common, while high-dose-rate temporary brachytherapy prescribed on rare occasions (Harvard Medical School, 2016). In the first few weeks after insertion, there is an increased risk of the pellets being discharged or displaced, thus men are advised to avoid exercise, beyond basic activities of daily living during this time period. Once a medical doctor has given approval, the survivor may resume exercise. Common side effects of brachytherapy can include: proctitis, dysuria, and hematuria; all of which generally resolve within a couple of weeks of treatment completion (Harvard Medical School, 2016).

Androgen Deprivation Therapy

Androgen Deprivation Therapy (ADT) is a common form of treatment for men with higher risk, advanced stage or recurrent prostate cancer (Ahmadi & Daneshmand, 2014). ADT may also be given to reduce the size of the cancer prior to other treatments. The goal of ADT is to lower the body's overall levels of testosterone and other androgens, and is delivered through medication or injectable drugs – primarily luteinizing hormone-releasing hormone (LHRH) agonists, gonadotropin-releasing hormone (GnRH) antagonists or anti-androgens (Harvard Medical School, 2016). ADT is associated with many adverse side effects, notably: negative changes in body composition, increased risk of cardiovascular, metabolic, and bone disease (Ahmadi & Daneshmand, 2014). There may also be significant declines in sexual health, health-related quality of life, and reduced functional capacity (Cormie et al., 2015). Exercise is recognized as a strategy to address these effects in men undergoing ADT therapy, specifically programs that focus on combining resistance and aerobic exercise at the moderate-to-high intensity level (Galvão, Taaffe, Spry, Joseph, & Newton, 2010).

Recent data has noted that there is an increased risk associated with ADT and cardiac specific mortality – especially for men with a history of cardiac disease (Ziehr et al., 2015). A meta-analysis of observational studies has shown a consistent positive association with use of ADT and cardiovascular disease related events (Bosco et al., 2015). For example, gonadotropin-releasing hormone agonists were associated with a 38% increased risk of non-fatal cardiovascular disease for men with prostate cancer when compared to men with prostate cancer on other treatments (Bosco et al., 2015). Orchiectomy and antiandrogens, other common forms of ADT therapy, reported a 44% and 21% increased cardiac risk respectively (Bosco et al., 2015). Furthermore, there was an association between ADT and early onset of a fatal myocardial infarction in men over the age of 65 having received treatment for 6 months or more (D'Amico et al., 2007). It is hypothesized that the increased risk is due to the reduced testosterone levels, resulting in increased levels of low-density lipoproteins, triglycerides, and insulin – all primary factors in metabolic syndrome (Su, Park, & Hsieh, 2014). Thus, there is a need for close monitoring of men on ADT at high risk of a cardiovascular event during exercise.

Physical activity and exercise

Exercise appears to be beneficial for men with prostate cancer; however, data is lacking on the optimal dose, duration, and mode of exercise (Bourke et al., 2016). Current evidence supports the benefit of exercise interventions for cancer-specific related quality of life, fatigue, and exercise capacity for men with prostate cancer; however, these results are largely from exercise trials examining men on androgen deprivation therapy (Bourke et al., 2016). Moreover, exercise prescriptions for prostate cancer survivors tend to fit a one-size-fits-all approach. Specifically, many studies follow the national exercise guidelines, examining aerobic and/or resistance training 2-5 times a week for 10-60 minutes per session, with the overall go of achieving at least 150 minutes of moderate-to-vigorous activity each week (Jones, Eves, & Scott, 2017). Despite differences in age, histology, and abilities, cancer participants are prescribed and follow generic exercise prescriptions (Jones et al., 2017). A generalized approach may fail to meet the unique physiological needs of the survivor, potentially resulting in an under dose or overdose of exercise training (Jones et al., 2017). Recommendations from a systematic review of exercise for prostate cancer survivors highlighted the need for exercise programs to be tailored to the individual's goals, physical limitations and capabilities (Bourke et al., 2015). Moreover, published guidelines from the American College of Sports Medicine roundtable on exercise for

cancer survivors recommend research examining exercise programs that tailor or adapt exercise based on the individual's physiological changes from treatment (Schmitz et al., 2010).

While generalized exercise programs may be advantageous for large trials and community settings, tailored exercise programs may be more beneficial in mitigating issues such as cancer-related cardiotoxicity, fatigue, and musculoskeletal issues. A generic exercise prescription may be problematic because it assumes the exercise load will have the same effects on the body systems for all individuals. As survivors with cancer are living longer, they are at risk for developing age-related conditions; specifically, cardiovascular disease (Benjamin et al., 2017). As an example, there is a paucity of research evidence examining the treatment or prevention of cardiovascular disease in relation to cancer. This type of research gap may be filled by personalized exercise programs. Closer attention to adaptations in exercise programs may better address side effects and decrease the chance of cardiovascular or other diseases, potentially improving patient-reported outcomes and overall well-being.

Although personalize exercise is recommended, few studies have examined the benefits of a personalized exercise program approach. Tailored exercise programs are currently being investigated to reduce fatigue in cancer survivors. One-third of cancer survivors are estimated to have clinically significant, persistent, cancer related fatigue (Jones et al., 2016). While there are multiple pathways in which exercise may improve cancer related fatigue, cancer survivors are unique in respect to different tumor types, treatments, and side-effects. Twomey (2018) published a study protocol examining tailored exercise interventions for individuals with persistent fatigue. The investigators propose to examine physiological parameters and pre-intervention data to inform the effectiveness of a tailored exercise program (Twomey, Martin, Temesi, Culos-Reed, & Millet, 2018). Specifically, they hypothesized that a more comprehensive understanding of an individual's health outcome goals, physiological parameters and sleep habits, will facilitate creation of a tailored exercise program, resulting in improved outcomes (Twomey et al., 2018).

Musculoskeletal issues are common in individuals over the age of 65 (Wolff, Starfield, & Anderson, 2013). With age, musculoskeletal tissues including bones, cartilage, ligaments, and muscles become more fragile, less resilient and elastic, and lose overall strength (Freemont & Hoyland, 2015). Exercise trials, with and without dietary components, have been shown to improve mobility and function in aging adults; however, there are currently no studies examining

the benefits of exercise for survivors of cancer with musculoskeletal impairments. Addressing musculoskeletal issues with a tailored exercise approach may improve adherence to exercise trials, while also improving overall health. Identifying the individual's optimal treatment regimen related to the specific frequency, intensity, time, and type of exercise, may ultimately improve the outcomes of exercise trials in the cancer area.

Summary

Prostate cancer has a high disease burden in terms of its negative impact on quality of life. Current evidence supports the benefit of exercise interventions for cancer-specific impairments and quality of life (Bourke et al., 2016); however, exercise prescriptions for prostate cancer survivors tend to fit a one-size-fits-all approach. Personalize exercise programs hold promise as a patient-centred care strategy to address a given cancer survivor's needs related to treatment, age, co-morbid conditions, and personal abilities.

CHAPTER 3: SCOPING REVIEW ON EXERCISE AND BONE METASTASES IN PROSTATE CANCER

Abstract

Purpose: This scoping review aims to synthesize the data on risks and risk mitigation associated with bone metastases in prostate cancer survivors, outline the potential benefits of participation in exercise, and provide guidelines to physiotherapists and exercise specialists for safe and effective exercise prescriptions.

Design: The stages implemented for the scoping review included: identifying the research question and relevant studies, study selection, charting the data, and summarizing the results. We searched the databases for systematic reviews, intervention trials, clinical practice guidelines, and survivor resources examining exercise for prostate cancer survivors with bone metastases.

Results: This review identified four clinical trials resulting in seven published journal articles relating to the potential safety and efficacy of exercise. The primary exercise prescription strategy to reduce bone risk involved avoiding the body region(s) with the metastatic lesion(s). Preliminary evidence from the studies supports the safety and benefit of supervised exercise in prostate cancer survivors with bone metastases.

Conclusion: Studies surrounding the safety and efficacy of exercise for prostate cancer survivors with bone metastases are limited. There is preliminary evidence that exercise is safe and beneficial for prostate cancer survivors living with bone metastases. Further research is warranted.

3.1 Introduction

3.1.1 Bone metastases and Prostate Cancer

According to Statistics Canada, prostate cancer is the most common cancer and is the third leading cause of cancer death from cancer among Canadian men (Canadian Cancer Society, 2016). It is estimated that in 2016, there were 21,600 new cases of prostate cancer in Canada, with approximately 59 men being diagnosed every day (Canadian Cancer Society, 2016). Compared to all solid tumor groups, prostate cancer has the highest prevalence of metastatic spread to the bone with incidence rates between 65 to 75 percent in advanced prostate cancer survivors (Coleman, 2001).

Bone metastases are commonly referred to as lytic, blastic (sclerotic) or mixed, depending on the radiographic appearance of the lesions. Osteo“lytic” bone lesions destroy the bone tissue and result when there is a pathological or abnormal active resorption of bone. Osteolytic lesions

present as “holes” or look like “punched out” regions of the bone. Alternatively, osteo“blastic” lesions are due to increased osteoblastic activity, where new bone is made without breaking down the old bone. As a result, while the bone is harder, the structure is not normal and the bone can break more easily (American Cancer Society, 2016). Mixed bone metastases are diagnosed when both blastic and lytic lesions are apparent on radiographic images (Coleman, 2001). The location of the bone metastases can vary due to the molecular and biological traits of the tumour cells; however, bone metastases in prostate cancer commonly affect the axial skeleton (spine), hip and pelvic regions.

3.1.2 Bone metastases and exercise

Exercise is recognized as an effective management strategy for men living with prostate cancer. Evidence has shown that exercise interventions improve cancer specific quality of life and cancer-related fatigue, as well as lower body strength and aerobic fitness (Bourke et al., 2016). Despite the positive effect of exercise, prostate cancer survivors with bone metastases are often excluded from exercise trials due to concerns over the potential for skeletal complications. These skeletal complications can include bone pain, fracture, or spinal cord compression. Currently, survivors with bone metastases report limiting their daily physical activity due to the fear of fracture, thus, further declining their overall health and increasing their risk of developing other comorbidities (Andriole, 2000). Despite the risks, current exercise prescription guidelines for cancer survivors recommend that even survivors with bone metastases should remain physically active (Schmitz et al., 2010).

Due to the higher risk of pathological fracture and spinal cord compression among survivors with bone metastases, knowledge on safe and appropriate exercise prescription is needed to inform practice.

3.1.3 Research Question

What are the benefits and risks associated with exercise for prostate cancer survivors with bone metastases?

3.1.4 Summary

This scoping review aims to present findings from clinical trials on exercise. No systematic reviews or clinical practice guidelines were found. Reviews that did not include a focus on both bone metastases and exercise (or physical activity) were excluded.

The main objectives were to (1) synthesize the data on safety of exercise for prostate cancer survivors with bone metastases, (2) outline the potential benefits of participation in exercise, and (3) provide guidelines to practitioners for safe and effective exercise interventions.

3.2 Methods

The stages implemented for the scoping review were based on recommendations from Levac et al., (2018) (1) identifying the research question, (2) identifying relevant studies, (3) selection studies for analysis, (4) charting and extracting the data, and (5) summarizing the results. The following electronic databases were searched in March 2017 and October 2018: PubMed, Web of Science, MEDLINE, and Sport Discuss. MEDLINE and PubMed were searched separately as PubMed is a search engine for MEDLINE. To account for unpublished research, major cancer and sports meetings were reviewed. Clinical trials details, unpublished thesis or dissertations were also reviewed. Furthermore, reference lists were searched for potentially relevant studies and authors were contacted if more information was necessary.

Keywords related to prostate cancer were used (e.g. prostate adenocarcinoma), bone metastases (ex. osteoblastic metastases, osteolytic metastases), exercise (e.g., physical activity, sport), and publication type (e.g. clinical trial, randomized controlled trial, controlled trial). These terms are presented in Appendix A.

A broad search strategy was used to scope the literature. The inclusion criteria included: (1) Publication between January 2000 and October 2018, (2) physical activity /exercise /stretching /physical manipulation in prostate cancer patients with bone metastases, and (3) Inclusion of one of the following outcomes: pain, fatigue, safety (adverse event rate), physical functioning, and quality of life. Exclusion criteria included: (1) non-human studies, and (2) Non-English language publications.

Titles and abstracts of relevant literature were reviewed and identified by one reviewer (KB) to remove articles that were clearly irrelevant. Two independent reviewers (KB and MM) screened the remaining literature against the exclusion/inclusion criteria. Information on the participants, methods, interventions and results were then extracted, recorded, and summarized. A total of six journal articles were included in this scoping review. See Appendix B for flow chart of the search strategy.

3.3 Results

A total of 14 journal articles were identified and, of these, seven were considered potentially relevant. Three of the journal articles discussed the same study cohort; therefore, only four trials are reviewed in this scoping review. The following information was extracted from each journal article: author, year, study design, participants, location of metastases, intervention, and the key findings. Data are provided in Appendix C.

3.3.1 Study details

The review identified four clinical trials (one before and after study, three randomized controlled trials) including a total of 111 men with prostate cancer and bone metastases. The average age ranged from 62.7 to 72.15 years. The total number of regions affected by bone metastases averaged 2.3 sites (±/-1.86), with one study not reporting the number of affected sites. Location of bone metastases included: pelvis, lumbar and thoracic spine, ribs, humerus, sacrum and other.

All the studies aimed to identify if an exercise intervention would be found safe and beneficial for men with prostate cancer and bone metastases. All four trials examined supervised exercise interventions and modified the prescription based on the location of the bone metastases. There was a focus on resistance training in the three of the studies. The resistance exercise prescription in two of the studies consisted of eight exercises targeting the major muscle groups in the upper and lower body. The weights and sets were increased every two weeks based on the participant's abilities. The third study required participants to complete four different resistance exercises in varying positions. These positions included: "all-fours," "gluteus arch," and "supine," with exercises focused on using the body as resistance rather than fitness or exercise equipment. Finally, the fourth study consisted of a multimodal exercise program (M3EP) including resistance, aerobic and flexibility. Training sessions were three times a week for around 60 minutes a session. Resistance training included major trunk, upper and lower body muscles, a 20 to 30-minute aerobic session at 60-85% of estimated heart rate maximum and, and static stretching.

The exercise interventions varied somewhat in duration. Three of the studies examined subjects over a 12-week period, with one study including a six-month follow-up after the 12-week intervention. One study examined exercise over a two-week period, while the survivors were receiving radiotherapy. After the two-week period, participants in this study were instructed to complete a six month, three days a week, self-directed exercise prescription at home.

3.3.2 Key findings

All studies assessed physical functioning, functional capacity, body mass, and quality of life. Improved physical function was observed through increased muscle strength and aerobic capacity, and improved ambulation. Body mass improved in all studies, with two studies showing increases in lean body mass and one showing significantly lower intra-abdominal fat. In one study that examined the effect of exercise during radiotherapy, no progression of metastases or changes in bone density were found. Progression of metastases and bone density were not examined in the other studies.

No adverse events related to skeletal complications were reported from exercise for any of the studies. There were three reported adverse events unrelated to the exercise sessions (i.e., advancing disease requiring chemotherapy, increased bone pain, and a fall).

3.4 Discussion

This scoping review found, that to date, there is limited research for prostate cancer survivors with bone metastases participating in exercise. Only four clinical trials were identified that examined prostate cancer and exercise; however, all showed similar results in terms of safety and benefits for physical functioning. While two studies also included breast cancer participants in their sample; no notable difference was reported between the two tumour types.

The studies included in this review showed improvement or maintenance of muscle strength and physical function. Furthermore, no skeletal events were reported, and bone pain was not exacerbated in any of the trials. Improvements in muscular strength and aerobic capacity can help protect against skeletal complications by improving overall physical fitness. Cormie et al., (2015) showed that the survivors involved in a 12-week trial were able to exercise at moderate-high intensity throughout the program, a level needed to obtain health benefits in the general population as well as in cancer survivors.

Men who have previously received ADT or are currently on ADT may be at risk of frailty due to muscle mass loss, weakness, and fatigue. While not all men with bone metastasis have received ADT, many of the frailty components are similar. None of the studies in this review showed benefit in terms of balance. Poor balance may lead to falls and injury, and falls and fall-related injuries can be life-threatening, especially among older persons (Stoyles, Borsch, & Alumkal, 2018). Thus, exercise to address muscle mass and education on fall prevention strategies may help to address symptoms of frailty and reduce the risk of falls (Stoyles et al., 2018)

Prostate cancer survivors with bone metastases are often inactive and if they are at high risk of, or sustain a fracture, by necessity may be placed on precautions, bed rest, or completely immobilized. During activities of daily living, muscles exert between 20-30 percent of maximal power, resulting in neither a decrease nor an increase in strength (Hettinger, 1994). Rief et al., (2014), had participants completing resistance exercises at 30-40 percent of maximal power, just above this threshold, which translated into self-reported increases in mobility and strength. Thus, improvements were reported even with lower intensities of exercise.

Bone strength reflects the combination of bone density and bone quality (Fonseca, Moreira-Gonçalves, Coriolano, & Duarte, 2014). Rief et al., (2014), showed that the major impact of resistance training in survivors with bone metastases was on bone density. The study completed by Rief et al., (2014), examined both prostate and breast cancer patients; however, did not separate the data by tumour type. Resistance exercise training has been shown to improve bone quality and bone density; however, studies to date, in the cancer area have been performed primarily with breast cancer patients (Dobek et al., 2011). Therefore, future research specifically with the prostate tumor group is needed. Moreover, bone density measurements are needed in survivors with confirmed bone metastases in order to evaluate the effect of exercise on bone integrity and bone strength.

Prostate cancer often generates sclerotic (osteoblastic) lesions that metastasize in the pelvis and axial skeleton (Lee, Saylor, & Smith, 2011). Only two of the studies discussed the specific location of lesion involved. Better reporting of bone lesion location is needed, as the exercise prescription and selection of exercise mode may be dependent on this factor.

Bone metastases are frequent in advanced prostate cancer cases, and are often associated with pain, functional impairments and decreased quality of life (Rief et al., 2014). Due to the small sample sizes, studies in the review were generally underpowered to detect quality of life improvements. Of note, in one study, patients reported feeling less worried about the loss of mobility and becoming dependent on others after the exercise program (Rief et al., 2014). In theory, improvements in functional ability may also increase the survivors' sense of self-control and self-esteem, resulting in less anxiety and fear of fracture (Rief et al., 2014).

Safety of the exercise programs was assessed by monitoring the incidence and severity of skeletal complications and adverse events during the exercise interventions. None of the studies reported any adverse events or skeletal complications; however, in general, the region of the bone

metastases was typically avoided in the exercise prescription. Given the low likelihood of adverse skeletal complications, especially in survivors with stable bone metastases, a larger sample is required to confidently conclude that exercise is safe.

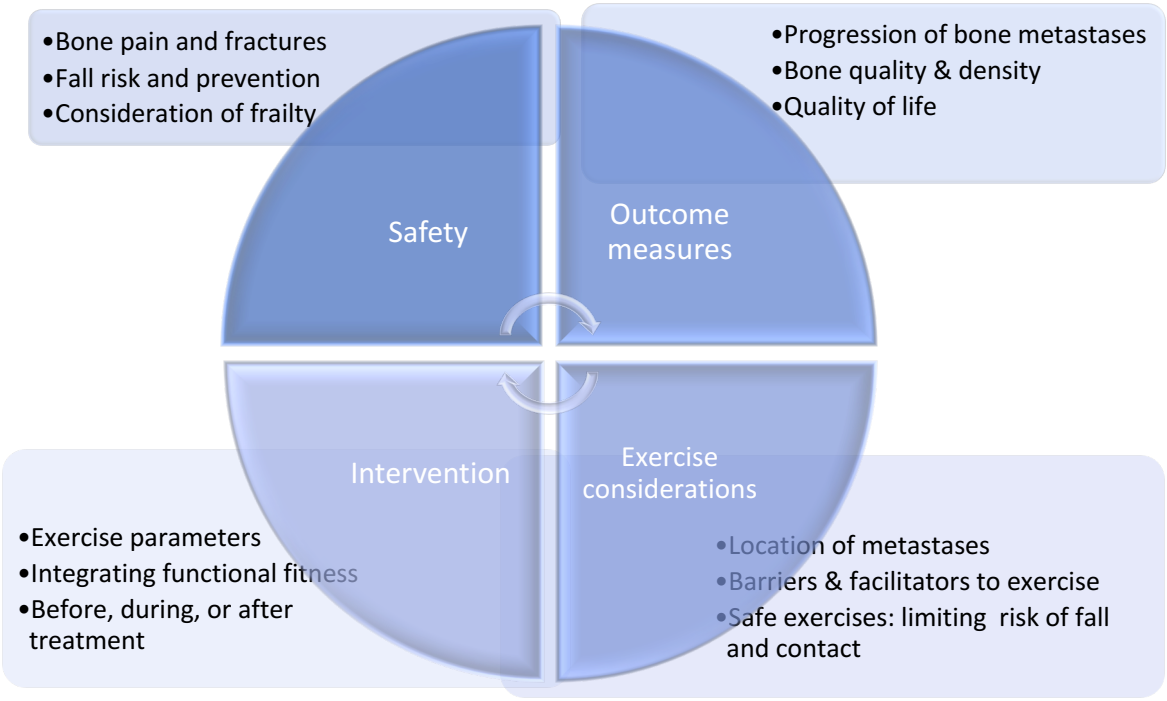
A recent study by Newton et al., (2018) compared different exercise regimens for men with prostate cancer undergoing ADT. While the study was not specific to men with bone metastases, the study did examine bone health. The results indicated that a clinical exercise program that includes targeted impact loading may be beneficial for the preservation of bone mineral density in the spine and hips (Newton et al., 2018).

This scoping review is limited by the small number of studies found examining exercise for men with prostate cancer and bone metastases. Thus, a broader focus including other cancer groups with bone metastases may be needed to fully evaluate the safety of exercise. Strengths include the extensive search of the literature and use of two independent reviewers. The studies included in this review provide preliminary evidence that exercise is well tolerated, safe, and improves physical functioning; however, larger control trials are necessary to confirm these results.

3.4.1 Future directions

As men are living longer with prostate cancer, bone metastases and disease progression may become a reality for more men. Future studies should address specific concerns related to bone metastases and prostate cancer. A summary tree outlining future considerations for this population can be seen in Figure 1.

Figure 1 Summary tree



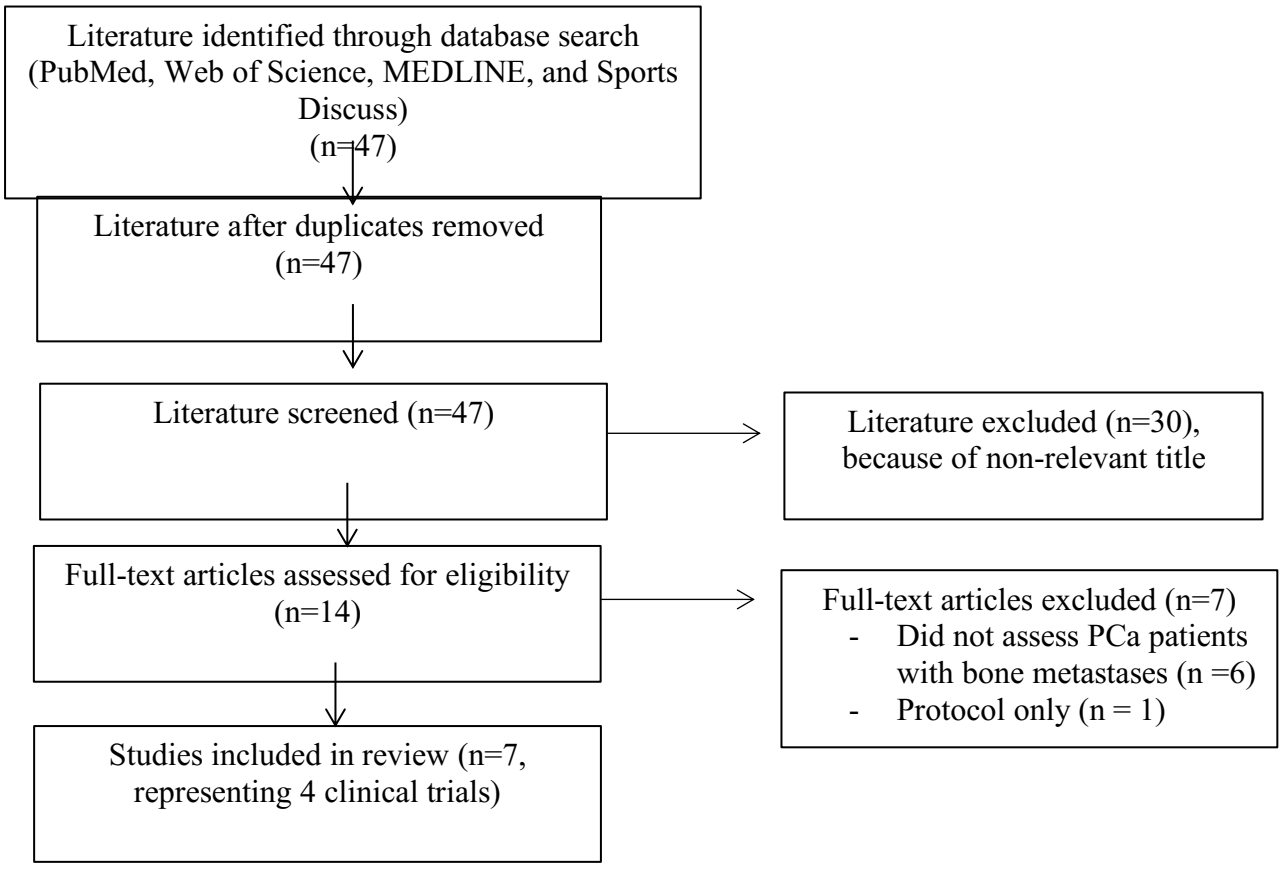
3.5 Conclusion

The literature on exercise for men with prostate cancer and bone metastases is limited. Initial research evidence supports that supervised exercise is safe and well tolerated, with exercise prescriptions largely avoiding the region of bone lesion. Future trials with larger sample sizes are needed to further explore the benefits and risks associated with exercise.

Appendix A

Database	Search Terms
PubMed	“Bone metastases and Prostate cancer” OR (“Bone Metastases"[All Fields] AND “prostate adenocarcinoma” OR “Prostate Cancer"[All Fields]) AND “exercise “or “physical activity” OR “aerobic activity” OR “resistance training” OR “Sport”
MEDLINE	Bone metastases and Prostate cancer and exercise or physical activity or aerobic activity or resistance training or sport
Web of Science	Bone metastases and Prostate cancer and exercise or physical activity or aerobic activity or resistance training or sport
Sport Discuss	Bone metastases and Prostate cancer and exercise or physical activity or aerobic activity or resistance training or sport

Appendix B


Literature identified through database search (PubMed, Web of Science, MEDLINE, and Sports Discuss) (n=47)
Literature after duplicates removed (n=47)
Literature screened (n=47)
Literature excluded (n=30), because of non-relevant title
Full-text articles assessed for eligibility (n=14)
Full-text articles excluded (n=7)
- Did not assess PCa patients with bone metastases (n =6)
- Protocol only (n = 1)
Studies included in review (n=7, representing 4 clinical trials)

Appendix C

Author/ year	Study Design	Participants	Location of metastases	Intervention	Key Findings	Key Measures (p-value)
Cormie, P. et al 2014	Single-group before and after study	20 men with stable bone metastases Age (years): 70.0 ± 9.8 Number of regions affected: 2.9 ± 1.9	Pelvis 21 Lumbar spine 12 Ribs/ Thoracic spine 14 Humerus 4 Other 7	3-month supervised resistance exercise program followed by a 6-motn observation period	Post-intervention Physical function (4-6%) Physical activity levels (160min/week) Lean mass (4-4%) 6-month follow-up Ambulation (4%) Physical activity level (105 min/week)	Physical function - Leg extension (0.291) - 6 min walk **(0.046)** - Timed up and go (0.915) - Balance (0.484) Body Composition - Lean mass **(0.039)** - Fat mass (0.833) Physical activity level (0.277) Fatigue (0.213)

Cormie, P. et al 2013	Two-armed randomized controlled trial	20 men with stable bone metastases Age (years): 72.15 ± 7.2 Number of regions affected: 2.65 ± 1.7	Pelvis 10 Lumbar spine 6 Ribs/ Thoracic spine 6 Other 3.5	12-week resistance exercise program (exercise based on location of bone lesions)	No adverse events or skeletal complications Exercise at target range for cancer survivors Increase maximal muscular strength, submaximal aerobic exercise capacity, ambulation	Physical function - Leg extension **(0.016)** - 400-m walk **(0.010)** - Timed up and go (0.150) - Balance (0.362) Body composition - Lean mass **(0.026)** - Fat mass (0.624)

Rief, H., et al 2014 Rief, H., et al 2014 Rief, H., et al 2014 Rief, H., et al 2014	Randomized controlled, trial	60 patients with stable bone metastases -multiple cancers Prostate cancer patients: 14 (5 in exercise arm) Age (years): 62.7 Number of regions affected: 1.4 (2-4)	Thoracic 15.5 Lumbar 11 Thoracic & Lumbar 2 Sacrum 1.5	Isometric resistance training or physical therapy	Improved functional capacity Reduced specific fears around loss of mobility and depending on other's for assistance Pain VAS was significantly lower both during and after RT in experimental No progression of other metastases in the vertebral column Fatigue and psychological stress decreased Bone density increased significantly by a mean of 28.3% (3 months) and 80.3% (6 months)	Fatigue - Physical fatigue **(0.013)** - Emotional fatigue (0.156) - Cognitive fatigue (0.433) - Daily life **(0.006)** - Social sequelae (0.363) Pain measurements - VAS **(<0.001)** - OMED **(0.018)** - Neuropathic pain (0.69)

Galvao, D., et al 2018	Two-armed randomized controlled trial	57 men with stable bone metastases Exercise (n=28) Age (years): 70.8 ± 8.4 Number of regions affected: Not reported	Pelvis 22 Femur 14 Rib/thoracic spin 18 Lumbar spine 13 Humerus 10 All regions 2 Other site 18	Modular multimodal exercise program (M3EP) Resistance, aerobic, and flexibility training	Muscle strength in lower leg significantly improved at 3 months Only 4 participants were able to complete baseline & 12-week chest press assessment Increased self-reported physical functioning No change in objective physical function, balance, lean mass, or total body fat mass No change in fatigue 89% attendance No exercise-related adverse events or skeletal fractures No changes in bone pain	Perceived physical function **(0.028)** Physical performance - Leg extension **(0.033)** - 6-min walk (0.192) - Up and go (0.497) Body composition - Lean mass (0.584) - Fat mass (0.598) Fatigue (0.964)

CHAPTER 4: METHODS AND PROCEDURES

4.1 Participants

A convenience sample of participants was recruited as part of the Alberta Cancer Exercise (ACE) study at the University of Alberta. All participants had previously taken part in the TrueNTH Exercise Program for at least one twelve-week session in the previous year. The men were given information about the study through a formal presentation to the support group and were provided with a pamphlet to take home. Interested participants were required to initiate contact with the investigators. This format enabled an efficient recruitment and allowed for a higher number of pilot study participants. Potentially eligible participants were screened for inclusion and exclusion criteria for both ACE and the prostate cancer sub-study.

4.2 Inclusion/ Exclusion criteria

The participants were included in the study if they met the following criteria: 1) histologically defined diagnosis of cancer, 2) on or off treatment or on surveillance for prostate cancer, 3) screened for exercise safety and approved for unrestricted exercise, and 4) were English speaking.

Participants were excluded from the study if they had 1) any musculoskeletal, neurological, or cardiovascular disorder deemed unsafe for exercise testing or intervention or 2) active metastatic disease where the condition posed a risk in terms of exercise testing or training.

4.3 Sample size

The sample size for this study was based on the hypothesis that a completion rate of greater than 80% would demonstrate feasibility of adherence to the personalized exercise program. On the basis of this hypothesis, if 20 participants were enrolled, at least 17 participants completed the study, the 95% confidence width for the proportion of successful adherence would be 22% (11-20 subjects). Accordingly, the minimum sample size for this study was 17 participants.

4.4 Study Design

The study was a single-arm before and after sub-study of the Alberta Cancer Exercise Hybrid Effectiveness-Implementation study. This sub-study was conducted to determine the feasibility and preliminary efficacy of implementing a personalized exercise program for men living with prostate cancer. This single-arm design was chosen as it allowed for a greater number of participants to enroll and potentially benefit from participation in exercise.

Feasibility was measured at both the level of the exercise specialist and the individual participant. For the exercise specialist, feasibility was established by calculating the time required to plan and conduct an exercise intervention, and arrange for any additional support or resources beyond general exercise testing and training. Feasibility for the participant was determined by calculating the attendance to exercise sessions, and adherence to the prescribed exercise workload.

Preliminary efficacy of the exercise program was determined by the following physical outcome measures: 1) functional capacity (six-minute walk test, sit to stand, and Unipedal stance test), 2) muscular strength (one-repetition maximum and grip-strength), and 3) anthropometric measures (height, weight, waist circumference, and hip circumference). All the participants had their baseline and final measures taken at the beginning of the study and after the 12-week exercise intervention.

4.5 Intervention

4.5.1 Baseline Evaluation

Participants who met the study eligibility were provided with information about the ACE prostate-specific program, which outlined the purpose, procedures, risks and potential benefits of participating in the program. The participants were also informed about the format including the group exercise circuit class and group personal exercise training. The participants provided written informed consent for both the ACE parent study and the prostate-specific sub-study.

Baseline evaluations were administered at the University of Alberta in the Cancer Rehabilitation Clinic. Data was collected and recorded on Baseline Data Collection Sheets (Appendix A) and the interview sessions were transcribed onto Interview Sheets (Appendix B). Data collection included the interview, PAR-Q, FACT-G, the Godin-Leisure Time Exercise Questionnaire, the six-minute walk test, sit to stand, unipedal balance, one-repetition maximum for lower and upper body, grip strength, height, weight, waist and hip circumference.

Interview

Prior to commencing the exercise program, participants were seen for a one-on-one interview to determine their personal goals for the program. Data was collected on issues that the participant felt might affect or represent a barrier to exercise participation, and their overall goals of exercise. This interview occurred at the beginning of the program to help inform the personalized exercise program. The questions and answers were recorded on a data collection sheet and health or musculoskeletal issues on a body-diagram.

FACT-G

The Functional Assessment of Cancer Therapy-General (FACT-G) is a quality of life measurement tool consisting of 34 items, with possible scores ranging from 0-108 (Cella et al., 1993). This instrument measures for dimensions of quality of life including: physical well-being, social/family well-being, emotional well-being, and functional well-being (Esper P et al., 1997). The questionnaire was filled out online through the REDCap system. Clarification on questions was provided as necessary.

Godin-Leisure Time Exercise Questionnaire

The Godin-leisure time exercise questionnaire was used to asses self-reported physical activity. The questionnaire contains three questions that assess frequency and duration of mild, moderate, and strenuous physical activity in a regular week within the last month. According to the Canadian Physical Activity Guide, a change of 30 minutes of activity per week is considered a clinically important difference (Zahavich, Robinson, Paskevich, & Culos-reed, 2012). The questionnaire was filled out online through the REDCap system. Clarification was given if necessary.

Six-Minute Walk Test (6MWT)

The 6MWT is a valid and reliable tool for measuring physical function and exercise capacity in a variety of patient populations including those with cardiovascular disease, the healthy elderly, and cancer patients (Schmidt, 2012). The 6MWT measures the distance the participant is able to walk over a six-minute time period on a 20-25-meter hard, flat surface. The participant walks at self-regulated pace and can rest at any point; however, the goal is for the participant to cover as much distance as possible in the six-minute time frame. The 6MWT assesses submaximal levels of functional capacity. As many activities of daily living are performed at submaximal levels of exertion, the 6MWT represents a metric of functional capacity. Furthermore, the test is considered safe, inexpensive, and easy to administer. Standardized procedures were used, and a data collection sheet was used during the test (see Appendix C).

Sit to stand (STS)

The STS test is a method to assess functional lower body strength in generally active, older adults. Additionally, the STS test is capable of assessing a wider range of functional skills, specifically any action that requires multiple repetitions (Jones et al., 2016). The STS measures the participant's ability to rise from a seated position in a chair to a full standing position (body

erect and straight) and return to a seated position as many times as possible. The final score is the total number of stands within a 30 second time period. Standardized procedures were followed (see Appendix D).

Unipedal stance test (UPST)

The UPST is considered a reliable and easy to perform assessment method for balance (Springer, 2007). Balance testing is useful in assessing variables associated with daily living such as frailty, gait and ambulation performance, safety, and fall risk. The UPST measures the participant's ability to stand on one foot under two conditions: eyes open and eyes closed. The maximal time for each test position (4 conditions: right, left, eyes open, eyes closed) is 45 seconds. Standardized procedures were used (see Appendix E).

One-repetition maximum (1-RM)

The gold standard for muscular strength assessments is considered the 1-RM in non-laboratory settings (Fleck & Kraemer, 2014). The 1-RM tests the highest load that can be lifted, one time, through full range of motion. The test is considered safe for populations including healthy adults, athletes, the elderly, and individuals with chronic disease (ACSM, 2014). The testing involved the bench press and leg press to measure upper and lower body strength respectively. Standard exercise machines were used for the testing. A warm-up including one set with a light weight was used to reduce the influence of learning or systematic bias (Hopkins, 2000). Standardized procedures were followed (see Appendix F).

Grip Strength

Grip strength is considered a simple, fast, and reliable measurement reflecting overall muscle strength and muscle mass (Wong, 2016). Grip strength norms and reference values have been established in order to help evaluate injuries, treatment goals, and assess the individual's ability to return to employment (Wong, 2016). To perform the grip strength test, a Jamar dynamometer was used, and measurements were recorded in kilograms (kg). Four measurements were taken, alternating between the dominant and non-dominant hands, and the best score for each hand was counted. Standardized procedures were used (see Appendix G).

Height and weight

Height was assessed using a stadiometer, a vertical ruler mounted on a wall with a wide horizontal headboard (ACSM, 2016). Height may vary slightly throughout the day due to the activity level of the participant, variation in fluid content in the intervertebral discs; therefore,

where possible, testing was performed at similar time period of the day and at the beginning of the testing session.

Weight was measured using a calibrated balance beam scale and moveable weights. Weight can also vary throughout the day due to exercise, hydration levels, meal/beverage consumption, urination, and clothing at the time of measurement. For consistency, participants were told to wear similar clothing for testing sessions, use the bathroom beforehand, and weight was recorded at the beginning of each testing session. Standardized procedures were used for height and weight measurements (see Appendix H).

Waist and Hip Circumference

Circumference measures can be used as an estimate of body composition and fat distribution and can inform disease risk and classification (ACSM, 2016). Measurement of waist and hip circumference is quick, easy and inexpensive. In order to ensure optimal accuracy two measurements of both the waist and hip were recorded as per recommended by ACSM. Standardized procedures were used (see Appendix I).

4.5.2 Exercise training program

Participants who met the eligibility requirements and consented to the study were required to exercise two times a week over a 12-week period. Exercise training consisted of one group circuit training session and one group personal training session, both involving aerobic and resistance exercise components. If a participant was unable to attend the group circuit training each week, they were scheduled for an additional personal training session. Participants were encouraged to perform additional exercise on their own at home or at another fitness facility on other days of the week.

The circuit training consisted of ten stations comprising resistance, aerobic, balance, and flexibility exercises. Each exercise session started with a structured warm-up or game activity and finished with a cool-down and stretching. The circuit training was timed with one minute and 15 seconds at each station, followed by a 10-15 second break. The circuit included two rounds of the circuit, with a three-minute break in-between each round.

During group personal training, the aerobic exercise intensity was set at an intensity of 12-14 on the Borg Scale of Perceived Exertion (representing approximately 50% of Maximal Heart Rate). Duration was set at 15 minutes for the first four weeks and increased by 5 minutes each

week from weeks 5-8 to a maximum of 30 minutes. As needed, the aerobic exercise was modified for the participant depending on how they were feeling that day.

The resistance training sessions aimed to enhance the muscular strength and endurance of all muscle groups. The muscle groups included: rhomboids (scapular retraction), levator scapula (scapular elevation), biceps (elbow flexion), triceps (elbow extension), quadriceps and hamstring (leg press and leg curl), and rectus / transversus abdominis (plank). Resistance was progressed throughout the 12-week period. Through weeks one to four, the resistance weight was set at 30-50% of 1RM, with an increase in intensity of ~5% biweekly. The men were asked to complete two sets of 10-15 repetitions for each resistance exercise. The group-personal training program allowed for some autonomy within the program. The men, in conjunction with the exercise specialist, modified the prescription (weights, repetitions, and sets) as necessary, depending on symptoms. Adherence to the exercise sessions and to the exercise prescription was monitored throughout the 12-week session. Adherence to the workload was considered successful if the participant completed $\geq$ 80% of the prescribed exercise workload including attendance, and variables of intensity, repetitions and sets.

The exercise specialist recorded the time required for planning and conducting the exercise program, and referral to other disciplines. The time was recorded on a calendar and summed for the 12-week session. This included the time required to create the circuit exercise class and the group personal training programs, set-up and takedown of each session, conducting the exercise sessions, and any additional time required to assist the participants before and after the sessions. All equipment that was used in each session and time was recorded on a data collection sheet as seen in Appendix K.

4.5.3 12-week Evaluation

After the 12-week intervention period, the participants completed a follow-up evaluation. The follow-up evaluation included the same testing as performed at baseline.

4.6 Data Collection

4.6.1 Primary Outcome

The primary dependent variable in this study was the feasibility of implementing a personalized exercise training program for men living with prostate cancer. For the purpose of this study, feasibility was measured at the level of the participant and at the level of the exercise specialist. Specifically, feasibility was measured at the level of the individual participant by

evaluating adherence to the prescribed exercise workload including attendance at sessions, and adherence to prescription variables of intensity, volume and time. Feasibility at the level of the exercise specialist was measured by documenting the time required to plan and conduct an exercise intervention as well as record the need for any additional resources beyond standard care.

4.6.2 Secondary Outcomes

The secondary outcomes in the study included examining the preliminary efficacy of physical fitness outcomes including: functional capacity (six-minute walk test, sit to stand, and unipedal stance test), muscular strength (one-repetition maximum and grip-strength), and anthropometric measures (height, weight, waist circumference, and hip circumference). Quality of life (FACT-G) and self-reported physical activity (Godin Leisure-Time Exercise Questionnaire) were also measured through the REDCap system.

4.6.3 Confounding variables

Physical activity levels may change due to increased symptoms such as decreased muscle mass, fatigue, and urinary or bowel dysfunction. We monitored the participants' symptoms and reasons for not attending exercise sessions; as well as encouraged the participant to stay active throughout the week, especially if they missed an exercise session.

4.6.4 Demographic information

Demographic information was obtained from the participant at the baseline assessment, including through questionnaires and personal interviews. Cancer-specific medical data included the stage of cancer and treatment of cancer (radiation, surgery, hormone therapy, and/or watchful waiting). Age, gender, marital status, education level, ethnicity, location of residence, income, and smoking and drinking status were also recorded.

4.6.5 Statistical analysis

An alpha level of 0.05 and a power of 80% were used for statistical analyses. The demographic information, consisted of interval and nominal data, was reported as the mean, standard deviation, and frequency/percentage respectively. The objective measures represent interval data, and due to the pilot nature of the study, are presented as the mean and standard deviation for the descriptive statistics. Furthermore, the inferential statistic was analyzed using a paired t-test to inform preliminary efficacy and the non-parametric Wilcoxon Signed-Rank Test to determine the significance of the findings.

4.7 Procedures

The study was conducted at The University of Alberta in the Cancer Rehabilitation Clinic (Corbett Hall) and the Foote Field Return to Activity Centre. At baseline testing, the participants completed the body composition, fitness and muscular strength tests. If the participant was unable to complete any of the tests, they were recorded as incomplete for that measure. The participants completed a 10-20-minute interview with the research coordinator to determine goals of the program, and exercise preferences, and potential issues related to participation. The participants also completed the FACT-G and Godin questionnaires in-person (paper version) or online through the REDCap electronic database. The exercise specialist developed the exercise prescription for both the group personal training program and the group circuit program. The participants booked an appointment for a 60-90-minute personal exercise training time once a week and were enrolled in the one-hour group circuit training class. Participants who were unable to participate in the group circuit training program completed a second 60-90-minute personal training session each week.

After the 12-week intervention, participants completed a post-intervention assessment; including the same body composition, fitness and muscular strength tests. The results of the baseline and 12-week post-testing were provided to the participants as requested. The study timeline is provided in Appendix M.

CHAPTER 5: RESULTS

5.1 Recruitment

Recruitment for the study began in April 2017 and was completed in May 2017.

5.2 Baseline Characteristics

A total of 24 participants were enrolled in the study, all males, with a diagnosis of prostate cancer. Baseline characteristics are shown in Table 1. The participants were on average 67.7 years old, and had a BMI of 29.1. Nineteen participants (79%) were classified as overweight or obese. All participants had been diagnosed with localized or locally advanced prostate cancer, and none had metastatic prostate cancer. Cancer treatments were as followed: 16 participants had received surgery, 12 radiation therapy and 15 had/ were undergoing ADT. Further demographic and medical information are outlined in Table 2.

Table 1. Baseline Patient Characteristics

Characteristics	n=24
Age (years)	67.7 $\pm$ 8.8
Caucasian	21 (87.5%)
Latin	2 (8.3%)
Asian	1 (4.2%)
Treatment received	
Surgery	5 (21%)
Radiation	1 (4%)
Hormone	3 (13%)
Surgery + radiation	1 (4%)
Surgery + hormone	2 (9%)
Radiation + hormone	2 (9%)
Surgery + radiation + hormone	8 (35%)
None	1 (4%)
Treatment Status	
Currently on ADT treatment	12 (50%)
On Radiation Therapy	2 (8%)
Off treatment	10 (42%)

BMI	29.1 ± 4.6

Table 2. Demographic Information

Demographics	n = 24
Education	
Some high school	1 (4%)
Completed high school	5 (21%)
Some university/ College	6 (25%)
Completed University/college	1 (4%)
Annual Family Income (n=20)	
<20,000	1 (4%)
20-39,999	1(4%)
40-59,999	4 (17%)
60-79,999	7 (29%)
80-99,999	3 (13%)
>100,000	5 (21%)
Marital Status	
Married/ common law	22 (92%)
Divorced/Separated	2 (8%)
Employment	
Working full-time	1 (4%)
Working part-time	1 (4%)
On long/ short-term disability	5 (21%)
Retired	17 (71%)
Smoking	
Never smoked	10 (42%)
Ex-smoker	12 (50%)
Occasional smoker	2 (8%)
Drinking	
Never drank	1 (4%)

Occasional drinker	11 (46%)
Social drinker	8 (33%)
Ex-drinker	3 (13%)
Regular drinker	1 (4%)

5.5 Interview

An interview was conducted with each participant at the baseline assessment. Consistent themes were found among participants. These themes helped to inform the group circuit class and personal training programs. Results from the interview can be seen in Table 3.

Table 3. Interview Results

Question	Responses	Themes	Proposed Strategy
Main identified barriers	• Musculoskeletal and other health issues: arthritis and pain (elbow, shoulder, low back, hip and knee; cardiovascular disease) (n = 16) • Lack of energy (n = 17) • Incontinence (n = 6)	Existing musculoskeletal and health issues Impairments related to treatment	1. Physiotherapy consult 2. Monitoring of fatigue before and after sessions 3. Incorporate pelvic floor retraining and cues into exercises; monitor leakage issues with specific exercises
3-5 Goals of your exercise program	• Increase muscle strength (n =13) • Increase energy (n = 8) • Keep body weight in control (n = 7)	Physical functioning: strength, balance, flexibility	1. Components of strength, balance and flexibility in standard program

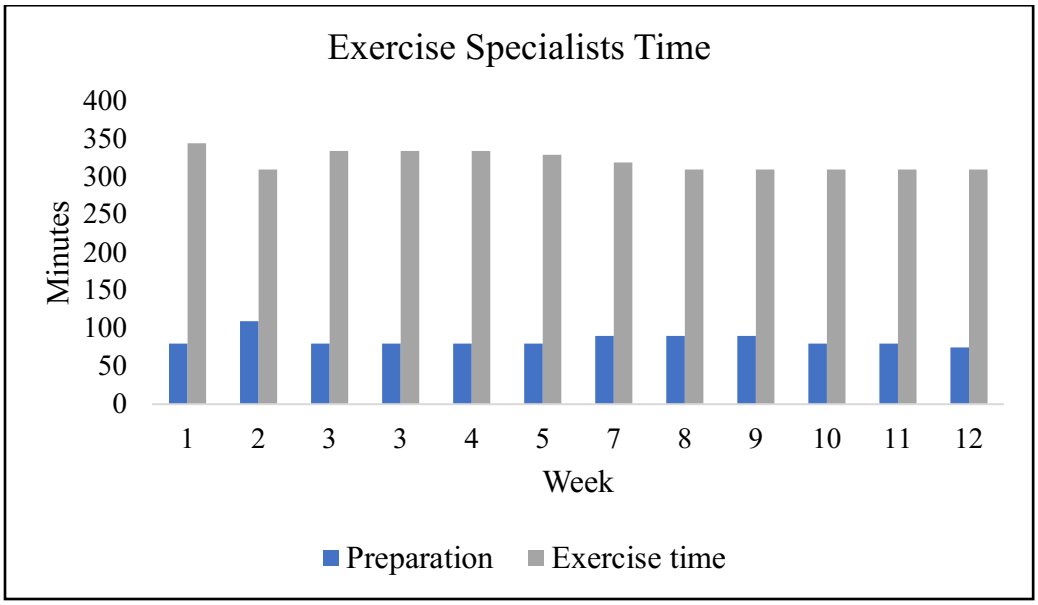
• Improve health/ disease control (n = 5) • Address incontinence (n = 4) • Reduce musculoskeletal pain (n = 3) • Increase flexibility (n = 3) • Improve balance (n =2) • Improve sleep (n =2) • Social interaction (n = 2) • Reduce depression and anxiety (n =2) • Improve bone density (n =1)	Impairments: fatigue, pain, incontinence, sleep Body composition: weight, bone density Health: disease control, musculoskeletal issues, depression and anxiety Social interaction	2. Monitor symptoms 3. Muscular strength-based focus; weight bearing exercises 4. Modifications to programming depending on existing issues 5. Group exercise programming

5.6 Primary outcome

5.6.1 Feasibility of the exercise specialist

The time needed to prepare the exercise programs and the actual training totaled 406.3 minutes or 6.8 hours per week. Each exercise session was led by an exercise specialist, supervised by an exercise physiologist or CSEP-CEP, with assistance from one-two rehabilitation medicine students. Preparation and exercise time can be seen on Figure 1. All equipment used for exercise was available on site. Additional resources and staff beyond a standard exercise facility were recorded. Scheduling and total time was recorded on a calendar app and resources were recorded on a separate spreadsheet through Microsoft Excel.

Figure 1: Exercise specialist total time



If participants had injuries or concerns they would first have a consult with the physiotherapist at the Cancer Rehabilitation Clinic. If necessary, the participant was referred to the student physiotherapy clinic or incontinence specialist for formal evaluation. The total estimated time for physiotherapy at the lab was ~133 minutes per week, provided in kind, at no cost. The total time estimated for physiotherapy at the student clinic was ~ 45 minutes per week costing a total of $320.00. The total estimated time for seeing an incontinence specialist was ~ 25 minutes per week with all costs being covered by Alberta Health Services (AHS) (Table 4). The additional true costs of service were $3643.43 (based on ~$67.00 per hour via current average Health Sciences Association of Alberta physiotherapy pay rates plus 23% estimated benefits). Thus, the average additional cost of providing this service was ~$150.00 per participant.

Table 4. Time and Cost for Services

Service	**Location**	**Type of treatment**	**Parti-cipants (n)**	**Visits/ parti-cipant**	**Time (mins)**	**Grant Costs**	**True Cost***
Physiotherapy	Cancer Rehab Clinic University of Alberta	Consult	16	1	20	In kind	$355.10
		Treatment	16	4	20	In kind	$1429.33
		Assessment	5	1	60	$100.00	$355.00

	Student Clinic	Treatment	3	4	60	$120.00	$804.00
Pelvic floor specialist	Referral to healthcare clinic	Assessment	2	2	60	100% AHS coverage	$200.00
		Treatment	2	3	60	100% AHS coverage	$500.00
					Total	**$320.00**	**$3643.43**

AHS: Alberta Health Services;

**Health Sciences Association of Alberta: physiotherapist average pay rate of $55.00 per hour plus benefits of ~23%.*

5.6.2 Feasibility of the individual participant

A total of 24 participants with prostate cancer enrolled in the study. All (n=24) completed the full 12-week intervention, baseline, and 12-week exercise testing. Two participants did not complete the 1RM test for the leg press at baseline: one due to shoulder pain (n=1), and the other due to recent brachytherapy with implantation of pellets before testing (n=1). The overall completion rate for the study was 100%.

Adherence to exercise intervention

An attendance rate of 87.0% was achieved for the group personal training sessions and 83.2% for the group circuit classes. Overall, the total adherence to the 12-week exercise program was 85.9% (Table 5.).

Table 5. Adherence to 12-week Intervention

	Group circuit training	**Group personal training**	**Total**
Participants	**Adherence**	**Adherence**	**Attended/ Scheduled**
	83.2%	87.0%	495 / 576 (85.9%)

Modifications to the exercise program were made for participants when necessary. Modifications included: 1) men who were unable to attend group circuit training due to physical limitations were scheduled an extra modified group personal training session, 2) modifications to exercise prescription: low back, shoulder, knee and hip safe exercise alternatives, 3) use of additional equipment and 4) treatment referral. The number of men completing the standard personal training program and a modified personal training program each week can be seen in Figure 2. Modification to the group personal training program can be seen in Table 6.

Figure 2. Standard versus modified personal training

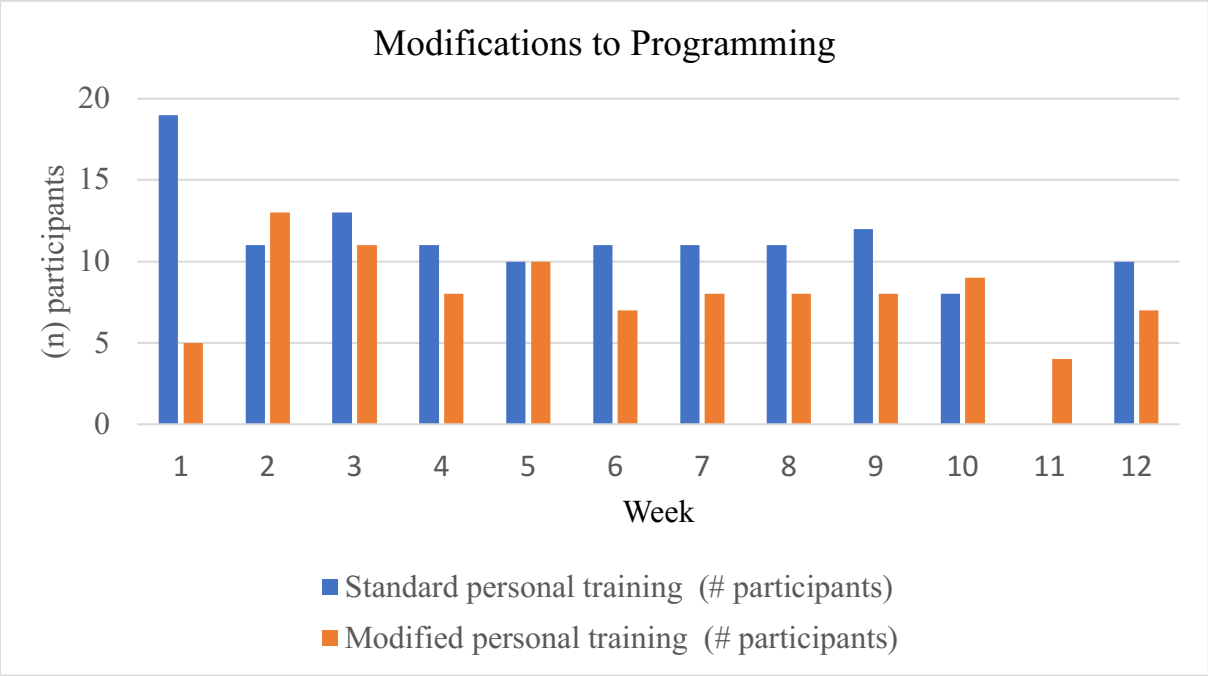


Table 6. Modifications to Training Program

	Issue	Modification
Training Method	Poor fitness/ scheduling	Group personal training only
	Incontinence	Addition of specialized pelvic floor exercises; avoidance of exercises causing excessive leakage, scheduled bathroom breaks
	Limited mobility	Use of raised plinth, seated exercise program

	(e.g. inability to get up and down from floor)	
Exercise modifications		
	Shoulder, knee, hip and low back issues	Physiotherapy: addition of ultrasound therapy, ice, and therapeutic exercises prescribed by physiotherapist; alternative "safe" exercises for circuit and personal training
	Pain with weightbearing/ Balance issues	AlterG treadmill Arm Ergometer Seated Elliptical
Referrals to other disciplines	Musculoskeletal issues Pain (shoulder n =2; Incontinence	Physiotherapy consult for modification (n =5) Physiotherapy treatment (n=3) Pelvic floor specialist (n=2)

Adherence to exercise workload

Adherence to the prescribed exercise workload was based on intensity, repetitions and sets. The goal of the program was to progress from 30-40% of 1RM to 60-70% by the end of the 12-week exercise session. Details on the calculation to determine intensity is provided in Appendix N. For upper body exercises, based on 1RM data for the chest press, adherence to intensity was 89.4%, with 100% adherence to repetitions and 100% adherence to sets. For lower body exercises, based on1RM data for the leg press, adherence to intensity was 83.4%, with 100% adherence to repetitions and 100% adherence to sets. Individual testing results, attendance, treatment and additional comments can be seen in Table 7.

Table 7. Adherence to Exercise Workload

Study ID	**1RM result**	**Intensity (% baseline / %12 week) (lbs)**	**Reps 10-12-15**	**2-3 Sets**	**Attendance**	**Comments**
E74 On ADT	Chest Press 70lbs – 70lbs	28.5% - 50% (20lb – 35lb)	100%	100%	95.8%	*Incontinence
	Leg Press	26.6% - 43.3% (40lb – 65lb)	100%	88%		

	150lbs – 150lbs					
E75	Chest Press 140lbs – 170lbs	32.1% - 54% (45lb – 75lb)	100%	100%	83.3%	*Left knee pain
	Leg Press 210lbs - 340	42.9% - 59.5% (90lb – 125lb)	100%	100%		
E76 On Radiation Therapy	Chest Press 140lbs - 163	28.6% - 35.7% (40lb – 50lb)	100%	100%	83.3%	*Incontinence issues; knee and shoulder issues
	Leg Press 205lbs - 220	43.9% - 53.7% (90lb – 110lb)	100%	92.3%		
E77	Chest Press 55lbs – 55lbs	29.1% - 40.9% (16lb – 22.5lb)	100%	100%	87.5%	*Shoulder, back and knee issues
	Leg Press 135lbs – 165lbs	51.9% - 66.7% (70lb – 90lb)	100%	100%		
E80 On ADT	Chest Press 100lbs -100lbs	40% - 45% (40lb – 45lb)	100%	100%	75%	Hip and groin issues, wrist & thumb osteoarthritis
	Leg press 220lbs – 220lbs	34.1% - 61.4% (75lb – 135lb)	100%	100%		
E82 On ADT	Chest Press 100lbs – 110lbs	30% - 55% (30lb – 55lb)	100%	100%	87.5%	Shoulder issues
	Leg Press 220lbs – 260lbs	54.5% - 75% (120lb – 165lb)	100%	100%		
E84 On ADT	Chest Press 45lbs – 50lbs	44.4% - 77.8% (20lb – 35lb)	100%	100%	91.7%	*Shoulder/knee/hip pain
	*Leg Press	NA	NA	NA		
E85 On ADT	Chest Press 120lbs – 120lbs	29.2% - 33.3% 35lb – 40lb	100%	100%	87.5%	*Back issues *Incontinence issues
	Leg Press 240lbs – 210lbs	18.8% - 21.9% 45lb – 52.5lb	100%	100%		
E87	Chest Press 95lbs – 80lbs	*40%-55% 40lbs – 52.5lbs	100%	100%	66.6%	*Incontinence NB: Viral infection last 3 weeks of exercise program.

	Leg Press 180lbs – 165lbs	40%-55% 70lbs-100lbs	100%	100%		
E90	Chest Press 140lbs – 150lbs	30%-65% 40lbs-90lbs	100%	100%	75%	*Back issues
	Leg Press 260lbs – 280lbs	35%-60% 90lbs-155lbs	100%	100%		
E91	Chest Press 82lbs – 120lbs	36.6% - 67.2% 30lbs – 55lbs	100%	100%	100%	
	Leg Press 210lbs – 220lbs	14.3% - 78.6% 30lbs – 165lbs	100%	100%		
E92	Chest Press 90lbs – 110lbs	50%-70% 45lbs to 65lbs	100%	100%	91.7%	
	Leg Press 220lbs – 240lbs	50% to 70% 110lbs-155lbs	100%	100%		
E93 On ADT	Chest Press 45lbs – 70lbs	44.4% - 55.6% (20lbs-25lbs)	100%	100%	100%	
	Leg Press 0lbs – 155lbs	NA – 38.8% (0lbs – 60lbs)	100%	100%		
E94 On ADT	Chest Press 140lbs – 150lbs	20% to 45% 30lbs-65lbs	100%	100%	83.3%	Shoulder, hip and knee issues Incontinence
	Leg Press 260lbs – 280lbs	26%-50% 70lbs-130lbs	100%	100%		
E95 On ADT	Chest Press 110lbs – 120lbs	27.3% - 45.5% (30lbs – 50lbs)	100%	100%	100%	
	Leg Press 280lbs – 280lbs	35.7% - 64.3% (100lbs – 180lbs)	100%	100%		
E96 On Radiation Therapy	Chest Press NA	(0lbs – 15lbs) Light resistance bands only	100%	100%	75%	*1RM deemed unsafe for participant due to Radiation Therapy *Balance and joint issues
	Leg Press NA	NA	NA	NA		

						*Incontinence
E97 On ADT	Chest Press 85-90	(0% to 35%) Light resistance bands to 35 lbs	100%	100%	100%	*Balance, mobility and shoulder joint issues *Incontinence
	Leg Press 140lbs-140lbs	Light weights and bands only	100%	100%		
E108	Chest Press 110lbs – 150lbs	54.5% - 68.2% (60lbs-75lbs)	100%	100%	87.5%	*Shoulder issues
	Leg Press 200lbs – 280lbs	45% - 67.5% (90lbs – 135lbs)	100%	100%		
E109	Chest Press 93lbs – 60lbs	Light resistance bands only	100%	100%	79.2%	*Shoulder and knee issues
	Leg Press 240lbs – 220lbs	Squats and body weight exercise only	100%	100%		
E110 On ADT	Chest Press 90lbs – 110lbs	Bands and light free weights	100%	100%	62.5%	*Balance issues *Shoulder, hip, and knee issues *Incontinence
	Leg Press 150lbs – 150lbs	Squats and body weight activities	100%	100%		
E113	Chest Press 95lbs – 110lbs	31.6% - 47.4% (30lbs – 45lbs)	100%	100%	95.8%	*Shoulder issues, abdominal hernia
	Leg Press 190lbs – 245lbs	50.0% - 76.3% (95lbs – 145lbs)	100%	100%		
E78	Chest Press 120lbs – 140lbs	30%-70% 30lbs-85lbs	100%	100%	83.3%	*Knee issues
	Leg Press NA	Body weight exercises only	100%	100%		
E83 On ADT	Chest Press 120lbs – 150lbs	20.8% - 50% (25lbs – 60lbs)	100%	100%	83.3%	*Cardiovascular issues: post stent X post 4 months
	Leg Press 200lbs – 200lbs	30% - 75% (60lbs – 150lbs)	100%	100%		

E86 On ADT	Chest Press 165lbs – 171lbs	30.3% - 60.6% (50lbs – 100lbs)	100%	100%	87.5%	*Precautions due to recent abdominal surgery (post 3 months)
	Leg Press 300lbs – 280lbs	30.0% - 53.3% (90lbs – 160lbs)	100%	100%		

5.7 Secondary Objectives

5.7.1 Preliminary efficacy of the exercise program

Table 8 illustrates the results from the baseline and 12-week post-intervention testing for the fitness and muscular strength outcomes of the study: functional capacity (six-minute walk test, sit to stand, and Unipedal stance test) and muscular strength (1RM and grip-strength). There were significant increases in both the 6MWT (p=0.04) and the sit-to-stand (p=0.005) test. As well, significant improvements were seen in upper and lower body strength through the 1RM bench press (p=0.02) and leg press (p=0.04). No significant differences were found for balance or grip strength.

The only anthropometric measure showing significant improvement was waist circumference. There were no significant improvements in weight, hip circumference, or BMI (Table 9).

Table 8. Functional Capacity Tests

n=24	**Mean (SD)**		**95% confidence interval**		**Paired sample t-test (2-tailed) P<0.05**
	Baseline	**12-week**	**Lower**	**Upper**	
Six-minute walk (meters)	558.3 (145)	575.0 (135.6)	500.3	616.3	0.04*
Sit-to-stand (amount)	17.2 (7.0)	19.5 (8.4)	16.1	22.8	0.003*
Unipedal Stance (seconds)	31.1(17.5)	32.0 (17.1)	25.1	38.8	0.87
Eyes open right	31.7 (15.7)	30.3 (15.0)	24.2	36.3	0.29
Eyes open left	5.8 (5.5)	5.3 (6.0)	2.8	7.7	0.61
	5.63 (6.8)	5.4 (4.0)	3.8	7.0	0.85

Eyes closed right					
Eyes closed left					
1RM bench press (lbs)	96 (36.9)	111 (36.4)	96.7	125.8	0.01*
1RM leg press (lbs)	193 (77.5)	221 (49.5)	200.9	240.5	0.04*
Grip strength (kg)	79.7 (20.8)	80 (22.4)	71.0	88.9	0.89

Table 9. Anthropometric Measures

n=24	**Mean (SD)**		**95% confidence interval**		**Paired sample t-test (2-tailed) P<0.05**
	Baseline	**12-week**	**Lower**	**Upper**	
Height	174.3 (7.1)	174.6 (7.4)	171.7	177.5	0.16
Weight	88.6 (16.8)	88.3 (17.6)	81.2	95.3	0.49
Waist circumference	103.7 (11.4)	101.5 (12.6)	97.3	108.5	0.02
Hip circumference	106.1 (9.2)	106.9 (8.7)	109.8	124.4	0.19
Waist-to-hip ratio	0.99	0.96			
BMI	29.1 (4.6)	28.9 (4.8)	27.0	30.8	0.32

5.7.2 FACT-G Questionnaire

Participants filled out the Functional Assessment of Cancer Therapy - General (FACT-G) on the REDCap data base. The mean total score at baseline was 76.9 and 77.8 at 12-weeks, with a mean difference of 0.9. No significant difference was found between scores over time (Table 10).

Table 10. FACT-G questionnaire

n=24	Mean (SD)		95% confidence interval		Paired sample t-test (2-tailed) P<0.05
	Baseline	**12-week**	**Lower**	**Upper**	
FACT-G total score	76.9 (16.4)	77.8 (15.3)	71.6	83.9	0.61

5.7.3 Godin Leisure-Time Exercise Questionnaire

Participants filled out the Godin Leisure-Time Exercise Questionnaire on the REDCap data base. Total exercise minutes were calculated with the primary outcome of examining the moderate-to-strenuous active minutes per week. The participants had an increase of 117.8 total moderate-to-strenuous minutes. Results from the questionnaire can be seen in Table 11.

Table 11. Godin Leisure Score Index

n=24	Mean (SD)			Paired sample t-test (2-tailed) And Wilcoxin Signed Rank Test
	Baseline	**12-week**	**Mean Change**	
Moderate-to-strenuous minutes	133.5 (131.3)	251.3 (217.3)	117.8 (149)	T-Test: $p < 0.001$ Wilcoxin: $p < 0.001$

5.8 Adverse events

No adverse events were reported during or following exercise testing or training.

CHAPTER 6: DISCUSSION

6.1 Feasibility

Feasibility outcomes suggest that offering an exercise program for men living with prostate cancer is safe and effective. Specifically, offering a personalized exercise program that includes group personal training and circuit class settings, exercise modifications, and clinical expertise allowed for high adherence. No adverse events occurred during the study. The completion rate for the study was 100%, with all participants completing the baseline and 12-week assessments.

6.2 Hypothesis related findings

6.2.1 Hypothesis related to feasibility

The participants would adhere to >80% of exercise sessions.

All metrics for adherence including recruitment, attendance and exercise variables of intensity, repetitions and sets exceeded 80%. Findings support the hypothesis that the program was feasible for men with prostate cancer. Previous studies have demonstrated feasibility of exercise programs for prostate cancer patients; however, this study was the first to examine the feasibility of a personalized exercise program for men with prostate cancer – with a specific focus on the men's individual exercise modification needs and goals. Examples of these needs included addressing and compensating for shoulder, knee and low back issues, incontinence, and symptoms of cancer-related fatigue.

There was a higher attendance rate for the group personalized exercise program when compared to the group circuit training class. High attendance rates are commonly reported in prostate cancer exercise interventions, with reported adherence rates ranging from 63% to 96% (Baguley et al., 2017). The men came into the study with a variety of health, musculoskeletal and osteoarthritic issues, and reported a lack of confidence in their ability to exercise given these limitations. Development of, or worsening of existing musculoskeletal issues in older adults are reported as the most commonly recorded minor adverse events in exercise interventions (Baguley et al., 2017). The main issues reported at baseline included: chronic low back pain, shoulder injuries, hip and knee pain, and joint stiffness. It was much easier for the men to pace themselves during the personal training sessions when compared to the circuit training class, and the men tended to rest, and extend their exercise sessions as needed. No new issues were developed as a result of the exercise intervention.

Resistance exercise intensity for the group personal training was prescribed using a percentage of the participants 1 RM achieved at baseline. The weight was monitored and adjusted, as necessary, throughout the program, progressing the weight depending on how the participant was feeling. High adherence to a prescribed exercise program for prostate cancer was also reported by Segal, et al. with 85.5% (Segal et al., 2017); however, overall, prescribed intensity of exercise is poorly reported among exercise interventions (Baguley et al., 2017). Data on exercise variables is critical to understanding outcomes and needed to inform the optimal exercise dosage.

The exercise program and in particular, the group circuit class provided a social environment for the participants. A sense of comradery developed among the men and information sharing was common. The high attendance rate may have been due to both the personalize exercise approach and the social interaction among the men.

We hypothesized that the time to plan and conduct an exercise intervention would not exceed 12 hours a week.

Our findings showed that, on average, the exercise specialist time per week was approximately 6.8 hours to plan and conduct a personalized exercise intervention for men with prostate cancer. The group personal training sessions were scheduled over a 3.5-hour period with 3-4 men exercising at any given time point. Originally, the men registered for specific 60-minute appointment time; however, through the course of the 12-weeks, the men became more independent and were able to attend at a time that worked best for their schedule within the half-day dedicated time period for the group. Preparation time for the group personal training programs ranged between 30-60 minutes. Preparation included creating the exercise prescription and modifying/ progressing the exercise plan weekly. We used a standard exercise format that included resistance training for all major muscle groups, an aerobic component, pelvic floor training, and cool-down/stretching following exercise. Physical abilities were determined through the baseline assessment, with weight being prescribed based on a percentage of the 1RM test. For example, if a participant completed a 150lb leg press, we prescribed a leg press at 40-50% of the 1RM (60lbs) for two sets of ten. Weight was increased throughout the 12-weeks on a weekly basis depending on symptoms and response to exercise.

The group circuit training program was scheduled once a week for 60-minutes at Foote Field. Class planning took on average 30 minutes, and the set-up of the equipment for the circuit

was done within 10 minutes. The class was planned by an exercise specialist and focused on resistance, aerobic, balance, and flexibility exercises, followed by a stretching and core exercise sequence at the end of the session. Each circuit consisted of 8-10 exercises, with two new exercises each week. Each exercise station included three options: easy (green), medium (yellow), hard (red), and safe positions to address joint pain and dysfunction were shared. This allowed the men to choose the level and modification of each exercise that worked best for them on that specific day. Modifications to each exercise were demonstrated at the beginning of class.

While the exercise specialist attended and coordinated all exercise sessions, other staff were available to assist participants. A physiotherapist or exercise physiologist was always on site as well as other graduate students assisting with exercises, treatment, and general inquiry from the participants. For the circuit training class, a CEP or physiotherapist provided onsite supervision, and an exercise specialist led the class with one or two rehabilitation medicine/ kinesiology practicum students assisting to ensure all exercise were done in a safe and effective manner. Thus, we were able to ensure a supervision ratio of 1 exercise specialist to 7-8 participants.

Interdisciplinary care has been recognized as a key component in providing best supportive care for cancer patients (Victorian Government, 2007). The interdisciplinary team approach is seen as beneficial in addressing the patients' physical, psychological, and supportive care needs. At the Cancer Rehabilitation Clinic at the University of Alberta, the team includes a physiotherapist, exercise physiologists, kinesiologists, and graduate students in occupational therapy, physiotherapy, speech language pathology, and rehabilitation science programs. As the personal training program was housed in the Cancer Rehabilitation Clinic, we were able to access physiotherapy services.

Two primary concerns of participants that were identified include incontinence and musculoskeletal conditions. Use of the body diagram brought attention to, and appeared to, help participants better identify musculoskeletal issues than existing screening tools. The physiotherapist and CEP discussed the exercise prescription, and a personalized modification to the exercise was provided to address limitations in joint movement and to avoid pain. The participants were monitored, during and following exercise sessions, to ensure the exercise program did not exacerbate the condition. Five participants were referred for further physiotherapy treatment or specialist care with three participants requiring physiotherapy treatment for joint related pain, and two requiring referrals for specialist assessment and treatment of incontinence.

Having access to an interdisciplinary team allowed for the men's needs to be addressed in a safe and timely matter. Physiotherapy treatments included additional ultrasound, cryotherapy and therapeutic exercises to assist with musculoskeletal issues. If physiotherapy treatment was necessary, the participant was scheduled for specific treatments in the adjacent Student Physiotherapy Clinic. The clinic has a variety of standardized physiotherapy and exercise equipment, which provided participants with options for both general and therapeutic exercise in terms of the equipment they used for exercise. A few of the men had difficulty getting up and down to the floor, where core and pelvic floor exercises were normally preformed. A raised plinth was available in the clinic for the participants to use as an alternative to the floor. The Alter-G treadmill (air supported treadmill) was also used for participants having difficulty with balance or joint pain with weight-bearing. This unique treadmill allowed participants, in need, to perform aerobic exercise safely and without pain. Physiotherapy bands were available as an alternative to the weight machines or dumbbells. If a specific exercise or piece of exercise equipment were problematic for a given participant, the physiotherapist or CEP would discuss options and determine a suitable alternative. This allowed individuals' exercise programs to be tailored to their specific needs and goals. The integrated team approach provided learning and educational opportunities, enhanced communication with patients, and resulted in improved quality of care for patients.

Although not all participants required interdisciplinary care, 67% of participants presented with multiple physical co-morbid conditions requiring modifications to exercise programming. Given a mean age of 66 years at the time of prostate cancer diagnosis, this finding is not surprising (Canadian Cancer Society, 2016). For those participants who were older, with more complex needs, the interdisciplinary team approach was seen as an asset, and allowed these individuals to stay with the exercise program. However, additional physiotherapy care at the clinic and the student physiotherapy services increased the cost of the programming. All costs at the student physiotherapy clinic and at the Cancer Rehab Clinic were covered by the study. While providing interdisciplinary care was feasible for the present study, covering physiotherapy costs in future programs may be problematic, especially in the community setting. The coverage of physiotherapy and additional care could have also positively influenced the attendance to the program.

6.2.2 Outcomes evaluating preliminary efficacy

We hypothesized that the exercise program would show trends towards better functional capacity, muscular strength, and anthropometric measures.

Functional capacity

The 6MTW and sit-to-stand both reported a significant difference in the 12-week intervention. There were no adverse events while completing the six-minute walk test and all men were able to complete the test at baseline and the 12-week assessment. Data on six-minute-walk distances for men with prostate cancer is limited in the literature; however, a study examining multiple cancer types reported a mean distance of 594.0 meters (Schmidt, Vogt, Thiel, Jäger, & Banzer, 2013). There are discrepancies in average 6MWT distances for the general population and cancer patients; however, when compared values seen in community-dwelling, 60-69 year-old males (572.0 meters), the participants in the present study walked slightly further (579.3 meters) (Steffen, Hacker, & Mollinger, 2002). While a statistical significance difference was found from baseline to 12-week testing, the distance of 17 metres did not reach the reported clinical meaningful difference of 10% or 30.5 metres (Bohannon & Crouch, 2017). The lack of a clinical meaningful difference may have been a result of the participants reaching a plateau due to already participating in an exercise intervention over the previous year, or due to negative effects of ADT treatment. Despite the lack of clinical significance, the increase in the six-minute walk may lend itself to an increased ability to participate in daily living activities and an increase in submaximal functional capacity.

There was a significant improvement in the participants' sit-to-stand test following the 12-week intervention. The sit-to-stand test has been shown as strong predictor of lower-body strength in older adults. In a previous study, men with advanced prostate cancer receiving ADT showed a mean improvement of 3.66 sit-to-stands, while another study with a primary focus of strength training for men with prostate cancer reported a mean improvement of 2.0 sit-to-stands (Nilsen et al., 2016) (Bourke et al., 2011). The present study showed a similar trend with a mean increase of 2.3 sits to stands.

Muscular strength

The resistance-training portion of the exercise program aimed to increase upper and lower body strength. A major finding of this thesis was the significant improvement in both upper and lower body 1RM. Both 1RM results were statistically significant showing 12-13% increases. These improvements exceeded the minimal clinically important difference of 10%. Moreover,

increases in strength were surprising given that participants had already been participating in an exercise program for at least one previous session and many were on ADT. Furthermore, the intervention only had one day a week of group personal training with a primary focus on progressive resistance exercise training. Findings thus differed from other prostate cancer studies. When compared to studies in Australia, the men had similar results in chest press 1RM; however, our leg press 1RM values were lower at both baseline and 12-week assessments (Galvão et al., 2010) (Cormie et al., 2015). The lower reported values for leg press may have been due to participant factors (e.g. existing osteoarthritis) or only having one resistance exercise training session per week. While other programs have two or three resistance training sessions each week, the present study offered a mixed approach of group personal exercise training and a group circuit class. While the circuit class included a resistance component comprising primarily body weight exercises (e.g. squats) and functional movement (e.g. up and down from floor), it was more difficult to progress the exercise intensity in a structured and mathematical way.

Improvements in grip strength did not reach statistical significance. When compared to healthy aged-matched Canadian's, the participants in the study had a lower mean grip strength of approximately 2.8 kg (Wong, 2016). Furthermore, when compared to the ACSM guidelines, the results for men of this age group would be interpreted as "fair" for healthy, aged-matched males (Pescatello, Arena, Riebe, & Thompson, 2006). Unfortunately, there is minimal data in the literature to inform grip strength norms for prostate cancer patients. Incorporation of grip strength in future studies may be helpful due to its established association with disability, morbidity, and mortality (Wong, 2016).

Anthropometric measures

The anthropometric measured in this study included height, weight, waist and hip circumference. One of the key findings was the significant decrease in waist circumference. While only a small insignificant weight loss was observed, the decrease in waist circumference may reflect a gain in lean muscle mass and a decrease of central fat mass. Regular physical activity is associated with a reduction of visceral fat, even if little to no weight loss occurs. Studies suggest that a significant reduction is visceral fat (10-19%) can occur with three months of regular physical activity, despite a lack of change in body weight (Ross & Janiszewski, 2008). Men with a waist circumference greater than 102cm are considered to be at a greater risk for cardiometabolic disease and all-cause mortality (Wang, Rimm, Stampfer, Willett, & Hu, 2005). The 2% reduction in waist

circumference observed in this study, translated in a reduction from 103.7cm to 101.5cm, placing these men, on average in a healthier classification. An approximate 3% reduction has been reported in other exercise trials; however, these studies included both men and women (Littman et al., 2012).

The waist-to-hip ratio is another measure of fat distribution in the lower and upper body. Health risks increase as the WHR increases, with a health risk value at >1.03 for men aged 60-69 years old (Wang et al., 2005). The WHR in this study showed a decrease from 0.99 to 0.96 throughout the 12-weeks, placing participants in the moderate risk category. The WHR is recognized to have limitations, in terms of estimating body fat; however, it provides informative data on the fat distribution of participants (Pescatello et al., 2006).

In the present study, a small non-significant improvement in quality of life was found. A systematic review and meta-analysis by Bourke et al., (2016) determined that there is high quality evidence stating that exercise can improve cancer specific quality of life in men with prostate cancer at 6 month follow-up. The mechanisms in which exercise influences quality of life are unclear; however, it is proposed that improvements in empowerment and self-efficacy may play a role (Bourke et al., 2016). Exercise studies that combine physical activity with a dietary component and combined lifestyle interventions show the highest improvement in quality of life scores for men with prostate cancer (Menichetti et al., 2016), suggesting interventions need to extend beyond exercise alone. Furthermore, there is mixed evidence determining which form of physical activity is most advantageous in improving quality of life. Cormie, et al. (2013) reported improvements in quality of life from resistance exercise training programs, while Monga et al., (2007) reported improvements with an aerobic training program. Segal et al., (2009), comparing the two modes of exercise, reported higher scores for quality of life in men that completed resistance training when compared to an aerobic training plan. Thus further research exploring which interventions are most effective will inform practice and implementation in the future (Menichetti et al., 2016).

Health – include?

To gain health benefits and improve physical function, it is recommended that adults accumulate at least 150 minutes of moderate-to-vigorous activity (in bouts of 10 minutes or more) each week (Canadian Society for Exercise Physiology, 2011). A total of 66 studies have examined the relationship between physical activity and functional abilities, independence, and cognitive function, showing a dose-response for intensity and volume of exercise (Canadian

Society for Exercise Physiology, 2011). Our participants reported an increase in moderate-to-strenuous physical activity of 117.8 minutes per week from baseline to post-intervention for a total of 251.3 minutes/ week at the 12-week assessment, exceeding the minimal important difference of 30 minutes. Even a low-dose of physical activity has been shown to reduce all-cause mortality risk in older adults, with further benefits seen with higher doses (Hupin et al., 2015). Throughout the study, the men were introduced to varying forms of exercise including different exercise machines, games, and individual exercises that could be done at a gym or at home. This exposure may have provided a means to learn new activities that are fun and safe. Many of the participants have continued to enroll in local exercise programming, as well as participate in yoga and walk/run groups.

6.3 Limitations

A limitation of this study was the small number of participants due to the pilot feasibility nature of the study. This study was also a single-arm intervention. An RCT design would be preferred to assess differences between exercise and usual care groups; however, the primary purpose of this study was to examine the feasibility of personalizing exercise in terms of exercise specialist time, resources and benefit to participants.

6.4 Sources of bias

The research investigator for the study had previously been the research coordinator for the TrueNTH program. The established relationship and trust, while allowing for better insight into the participants needs and abilities, may have resulted in improved adherence. As well, many of the participants had developed relationships with one another, and a positive and vibrant group dynamic was evident. Moreover, the participants had participated in the TrueNTH program for at least one session in the previous year; therefore, they were all familiar and comfortable with the equipment and time requirements to participate in a bi-weekly exercise program.

6.5 Future directions

Research in cancer and exercise is increasing exponentially. Closer attention to the monitoring of, and reporting of adherence to exercise prescription variables of intensity, frequency, and duration may better inform dosage of exercise needed to obtain benefit. Our findings suggest that many prostate cancer survivors, especially those with other health and musculoskeletal issues, may be in need of, and benefit from a personalized exercise approach. Future studies are needed

examining the benefits, including cost benefits, of an interdisciplinary approach to personalizing exercise.

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APPENDIX

A. Consent form
B. Baseline data collection sheet
C. Interview and body diagram
D. Six-minute walk test
E. Sit-to-stand test
F. Unipedal stance test
G. One-repetition maximum test
H. Grip strength
I. Height and weight
J. Waist and hip measurements
K. Time and resources
L. Data collection sheet
M. Timeline
N. Intensity calculation

Appendix A

Consent Form

Consent form

Informed Consent Form for Participation in a Research Study

The Alberta Cancer Exercise "ACE" Program for Cancer Survivors Supporting Community Based Exercise Participation for Health Promotion and Secondary Cancer Prevention

(A study to evaluate the benefit of a community-based exercise program for cancer survivors)

Protocol ID: *HREBA.CC-16-0905*

Principal Investigator: Dr. Margaret McNeely, PT, PhD
Department of Physical Therapy/ Department of Oncology
University of Alberta & Cross Cancer Institute
Phone: 780-248-1531

Sponsor/Funder(s): Alberta Innovates Health Solutions

Emergency Contact Number (24 hours / 7 days a week):
Cross Cancer Institute Telephone Triage Nurse:
780-432-8919 or 1-877-707-4848 (toll free)

You are being invited to participate in a research study because you have you have indicated that you are interested in participating in a community-based exercise program for survivors of cancer. This consent form provides detailed information about the study to assist you with making an informed decision. Please read this document carefully and ask any questions you may have. All questions should be answered to your satisfaction before you decide whether to participate.

The study staff will tell you about timelines for making your decision. You may find it helpful to discuss the study with family and friends so that you can make the best possible decision within the given timelines.

Taking part in this study is voluntary. You may choose not to take part or, if you choose to participate, you may leave the study at any time without giving a reason. Deciding not to take part or deciding to leave the study will not result in any penalty or any loss of medical or health-related benefits to which you are entitled.

The principal investigator, who is one of the researchers, or the site research coordinator will discuss this study with you and will answer any questions you may have. If you do consent to participate in this study, you will need to sign and date this consent form. You will receive a copy of the signed form.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

The growing population of cancer survivors in Alberta has brought attention to the long term toll of cancer and its treatment on the body, mind and overall health of survivors. Exercise is an effective intervention that can optimize the health and wellbeing of cancer survivors and possibly reduce rates of cancer recurrence and secondary cancers. Currently standard care at the Cross Cancer Institute is to receive counseling on the value of physical activity and healthy living after the completion of cancer treatments.

The Health Research Ethics Board of Alberta – Cancer Committee (HREBA-CC), which oversees the ethical acceptability of research involving humans, has reviewed and granted ethics approval for this study.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to evaluate the benefit of a community-based exercise program for cancer survivors. The program is called the Alberta Cancer Exercise (ACE) Program. Our aim is to support persons who have been diagnosed with cancer to adopt an active lifestyle in order to

improve their health outcomes. We want to see whether survivors are interested and able to take part in the program and if outcomes are similar to those seen in supervised research studies and hospital-based programs. We also plan to study how best to implement the program in the different community-based exercise facilities across Alberta.

WHAT ARE OTHER OPTIONS IF I DECIDE NOT TO PARTICIPATE IN THIS STUDY?

You do not have to take part in this study in order to receive continued medical care. You may choose not to participate in this study. Your healthcare provider will discuss lifestyle recommendations with you. Right now, the usual treatment at the Cross Cancer Institute is to receive counseling on the value of physical activity and healthy living after the completion of cancer treatments.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 1000 people across Alberta will take part in this study. We plan to enroll about 350 people at the Cross Cancer Institute.

WHAT WILL HAPPEN DURING THIS STUDY?

STUDY INTERVENTION

If you agree to take part in this study, you will undergo screening and fitness testing and will be referred to a suitable exercise program. The exercise program will take place at selected sites including Edmonton YMCAs and Wellspring. You will take part in a twice weekly exercise program for a 12-week period and will be followed for study outcomes for up to a year. The exercise program will be tailored to your fitness level and designed to address your personal fitness or lifestyle goals.

If you are a survivor with prostate cancer, you will have the option to take part in exercise programming that is tailored to your specific needs and offered in a group setting with other

prostate cancer survivors. Exercise programming will have a specific focus on resistance exercise and incorporate pelvic floor exercises along with aerobic, balance, coordination and flexibility exercises.

All participants will have measurements taken at the start of the study, at 12-weeks, 24 weeks and at one year to see the effect of exercise on their physical activity levels and quality of life. Participants taking part in the study will have the option to receive a follow-up questionnaire after completing the exercise program each year for up to 5 years (remaining length of the study).

STUDY PROCEDURES

Established Procedures

The following established procedures will be done as part of this study. Some of these procedures may be done as part of your standard care, in which case the results may be used. Some may be done more frequently than if you were not taking part in this study. Some of these procedures may be done solely for the purpose of the study. If the results show that you are not able to continue participating in the study, the principal investigator will let you know.

- Body composition measurement: We will measure your height and body weight. As well, we will take a measurement of your waist and hip size with a tape measure. These measurements take between 2 and 3 minutes to complete.

- Aerobic endurance measurement: We will have you perform a 6-minute walk test in a hallway on a flat surface to determine your fitness level. This is a submaximal test, meaning that you will walk at a moderate pace for the 6-minute time period. The walk test takes around 10 minutes to complete.

- Musculoskeletal fitness measurement: we will measure your grip strength, measure your lower body endurance (30s Sit to Stand), and assess your flexibility using a sit-and-reach test and shoulder elevation measure. We will also assess your balance using a one-legged stance balance test. These tests take around 20 minutes to complete.

- Optional fitness tests: Depending on your interests and the location of your exercise program you may have the option to undergo additional fitness testing including the following: Push-up test (upper body muscular endurance); Plank test (core endurance); a submaximal/ maximal strength test for your arms (bench press) and your legs (leg press); a submaximal cycle or treadmill test (meaning that you will exercise at a moderate level until you reach a specific heart rate. This test helps us to better estimate your fitness).

- Optional test if you have cancer fatigue: if you have fatigue due to your cancer or cancer treatment, you will have the option to undergo a muscle fatigability test. In this test, we will see how quickly your thigh muscle tires when exercised. If you choose to perform this test, you will need to return for an additional testing session. This additional visit will take around 30-60 minutes.

<u>Questionnaires</u>

You will be provided with a questionnaire package at the start of the study, at 12 weeks, at 24 weeks, and at one year. You will have the option to complete the follow-up questionnaire package each year for the duration of the study (up to 5 years). The purpose of the questionnaire is to understand how the program affects different aspects of your life.

- The revised Edmonton Symptom Assessment Scale : this questionnaire asks you to rate symptoms related to your cancer and cancer treatment. This questionnaire is usually administered as part of your standard care. This questionnaire takes about 5 minutes to complete.

- Stage of Change (at start of study only): This questionnaire asks about your readiness to take part in exercise. This questionnaire takes 1 minute to complete.
- Exercise preferences questionnaire (at the start of the study only): This questionnaire asks about your exercise goals and the type of exercises you would like to take part in. This questionnaire takes 1 minute to complete.
- Physical activity level: We will ask you about your physical activity level using the Godin Exercise Leisure-time Questionnaire. This 6-item questionnaire asks specific questions about the type, intensity, frequency and duration of your average weekly physical activity. This questionnaire takes around 2-3 minutes to complete.
- Cancer-related Quality of Life: We will assess your quality of life using the Functional Assessment of Cancer Therapy-Fatigue Scale. This 39-item questionnaire asks specific questions about the impact of your cancer and cancer treatment on your physical wellbeing, social/family wellbeing, emotional wellbeing, functional wellbeing and fatigue. This questionnaire takes around 10 minutes to complete.
- Health-related Quality of Life: We will assess your quality of life using the RAND short form (SF)-36. This 36-item questionnaire asks questions about your general health including physical functioning, pain, limitations, emotional wellbeing, social functioning, energy, general health perception and preveived change in health. This questionnaire takes around 10 minutes to complete.
- Cost effectiveness: We will assess the cost effectiveness of the program using the EQ5D. This 5-item questionnaire asks questions about your mobility, self care, usual activities, pain/discomfort and anxiety/depression. This questionnaire should take 2-3 minutes to complete.

The information you provide is for research purposes only and will remain strictly confidential. Some of the questions are personal; you may choose not to answer them.

Even though you may have provided information on a questionnaire, these responses will not be reviewed by individuals not involved in this study, e.g., your health care practitioner/team. If you would like them to know this information, please bring this to their attention.

Participant Diaries

You will be asked to keep a diary of your daily physical activity during the 12 week exercise program. This will include recording the type of physical activity, the duration and intensity of each session and any symptoms before or after each session. You will be asked to return the diary at your 12-week follow-up test at the Cancer Rehabilitation Clinic in Corbett Hall at the University of Alberta, or to submit an electronic copy to the researchers.

WHAT ARE THE POTENTIAL SIDE EFFECTS FROM PARTICIPATING IN THIS STUDY?

You may experience side effects from participating in this study. Some side effects are known and are listed below, but there may be side effects that are not expected. You should discuss these with the principal investigator or research coordinator. The risks and side-effects of the standard or usual treatment will be explained to you as part of your standard care. These risks are not included in this consent form.

The main side effect from exercise testing and training is secondary muscle soreness. You may notice that your muscles are sore for a couple of days after the testing session and during the first week or so of the exercise program. We expect that these symptoms will get better as you get used to the exercise. As well, the exercise program will be personalized to you to minimize excessive soreness and modified as needed if you experience any excessive muscle soreness or fatigue from your exercise sessions.

It is important that you know and understand the possible risks of the treatments given in this study. The main risk associated with exercise is musculoskeletal injury (injury to the muscles, tendons, joints or bones). Your exercise sessions will be supervised and your program designed to minimize this risk by slowly increasing the amount and intensity of your exercise over time.

There is also a very small risk of heart issues (such as chest pain, irregular heart rate, heart attack) should you exercise too intensively. To avoid any risks associated with exercise, you will be screened to ensure it is safe and appropriate for you to take part in the exercise program. All exercise will be of a low to moderate intensity level to minimize the stress on the heart and body. As well, we will monitor your vital signs (e.g., heart rate, blood pressure) during the exercise testing and if needed, when you exercise at the participating facilities. If any concerns are identified at any time, you will be referred back to your doctor for further evaluation. If any issues develop during the study period, your exercise sessions may be held or discontinued.

If you have any side effects, you should call the principal investigator or study coordinator in charge of the study. The telephone numbers are on the last page of this form.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

Participation in this study may or may not be of personal benefit to you. Possible benefits include improved physical fitness and better energy. Based on the results of this study, it is hoped that in the long-term, patient care can be improved.

WHAT ARE MY RESPONSIBILITIES AS A STUDY PARTICIPANT?

If you choose to participate in this study, you will be expected to:

- Tell the study research coordinator about your current medical conditions;
- Tell the study research coordinator about all prescription and non-prescription medications and supplements, including vitamins and herbals, that you may be taking and check with the research coordinator before starting, stopping or changing any of these. This is for your safety as these may interact with the intervention you receive on this study;
- Tell the study research coordinator if you are thinking about participating in another research study;
- Attend all scheduled study visits, undergo all of the procedures described above and

complete the questionnaires.

- Inform the study research coordinator of any injuries, side effects or health problems that you may be experiencing

HOW LONG WILL I BE PARTICIPATING IN THIS STUDY?

The study exercise program will last for about 12 weeks. You will be asked to come back to the Cancer Rehabilitation Clinic in Corbett Hall at the University of Alberta for follow-ups at 12-weeks, 24 weeks and one year. Each follow-up testing session will take around an hour and a half (90 minutes) to complete. In addition, you will have the option to complete the questionnaire once a year for up to 5 years.

WILL THERE BE ANY LONG-TERM FOLLOW-UP INVOLVED WITH THIS STUDY?

If you stop receiving the study intervention early, we would like to keep track of your health for up to the one year study period to look at the long term effects of the exercise intervention on your health. We would do this by having you come back to the Rehabilitation Clinic in Corbett Hall at the University of Alberta for the fitness assessments and/ or by completing the questionnaire.

In the event it is necessary to further evaluate the safety or efficacy of the community-based cancer exercise program it may be necessary to have access to additional information about your health status. The study team may attempt to obtain study-related information about your health from you or from other private sources, including your care physician. This may include contacting you again by phone or letter, but only if you have not withdrawn your consent for future contact. However, contacting you, your care physician or using other private sources of information, is optional, please indicate your decision using the check boxes below.

You give permission to the study research coordinator or member of the study team to attempt to obtain study-related information about your health status to further evaluate the safety or efficacy of the community-based cancer exercise program. This may include contacting your care physician, or by contacting you by phone or letter (i.e., future contact).

☐ Yes ☐ No Participant's Initials: _____

Name/phone number of care physician: _____

CAN I CHOOSE TO LEAVE THIS STUDY EARLY?

You can choose to end your participation in this research (called early withdrawal) at any time without having to provide a reason. If you choose to withdraw early from the study without finishing the intervention, procedure or follow-up, you are encouraged to contact the principal investigator or research coordinator. If you decide to stop participating in the study, we encourage you to talk to your doctor first. You may be asked questions about your experience with the study intervention.

You may withdraw your permission to use information that was collected about you for this study at any time by letting the research coordinator know. However, this would also mean that you withdraw from the study. Information that was recorded before you withdrew will be used by the researchers for the purposes of the study, but no additional information will be collected or sent to the sponsor after you withdraw your permission.

CAN MY PARTICIPATION IN THIS STUDY END EARLY?

In discussion with you, your doctor at the Cross Cancer Institute, either at his/her own initiative or at the request of the sponsor of this study, may withdraw you from the study at any time if it is in your best interests.The principal investigator may stop your participation in the study early, and without your consent, for reasons such as:

- You are unable to tolerate the exercise.
- You sustain an injury as a result of participation.
- You experience an adverse effect during or after exercising.
- Your doctor no longer feels this is the best treatment for you.
- The sponsor decides to stop the study;

If this happens, it may mean that you would not receive the study intervention for the full period described in this consent form. If you are removed from the study, the principal investigator will discuss the reasons with you and plans will be made for your continued care outside of the study.

HOW WILL MY PERSONAL INFORMATION BE KEPT CONFIDENTIAL?

If you decide to participate in this study, the principal investigator and study staff will only collect the information they need for this study.

Records identifying you, including information collect from your medical files/records, such as your Electronic Medical Records (EMR), Netcare, charts, etc., will be kept confidential to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

Authorized representatives of the following organizations may look at your identifiable medical/clinical study records at the site where these records are held for quality assurance purposes and/or to verify that the information collected for the study is correct and follows proper laws and guidelines:

- The Health Research Ethics Board of Alberta – Cancer Committee, which oversees the ethical conduct of this study
- Members of the Regulatory/Audit team at the Cross Cancer Institute, for quality assurance purposes

Authorized representatives of the above organizations may **receive** information related to the study from your medical/clinical study records that will be kept confidential in a secure location and may be used in current or future relevant health research. Your name or other information that may identify you will not be provided (i.e., the information will be de-identified). The records received by these organizations will be coded with a number. The key that indicates what number you have been assigned will be kept secure by the researchers directly involved with your study and will not be released. To protect your identity, the information that will be on your assessment forms and questionnaires will be limited to your study ID and initials.

Any disclosure of your identifiable health information will be done in accordance with federal and provincial laws including the Alberta Health Information Act (HIA). The organizations listed above are required to have organizational policies and procedures to protect the information they see or receive about you, except where disclosure may be required by law. The principal investigator will ensure that any personal health information collected for this study is kept in a secure and confidential AHS facility as also required by law.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during the study will be used in analyses and will be published and/or presented to the scientific community at meetings and in journals, but your identity will remain confidential. It is expected that the study results will be published as soon as possible after completion. This information may also be used as part of a submission to regulatory authorities around the world to support the approval of this intervention.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated. Every effort will be made to keep your identifiable information confidential, and to follow the ethical and legal rules about collecting, using and disclosing this information.

Data collected will be entered into the secure RedCap server held at the University of Alberta and data will only be used for research purposes.

Studies involving humans sometimes collect information on race and ethnicity as well as other characteristics of individuals because these characteristics may influence how people respond to different interventions. Providing information on your race or ethnic origin is voluntary.

WILL MY HEALTHCARE PROVIDER(S) BE INFORMED OF MY PARTICIPATION IN THIS STUDY?

Your family doctor/health care provider will be informed that you are taking part in a study so that you can be provided with appropriate medical care. If you do not want your family doctor/health care provider to be informed, please discuss with your study team to find out your options.

WILL THERE BE ANY COSTS INVOLVED WITH PARTICIPATING IN THIS STUDY?

You will not have to pay for the exercise program you receive in this study. We will provide a parking pass to cover your parking costs at the University of Alberta when you come for any tests or procedures associated with the study. Costs associated with attending the 12-week exercise program in the community will be covered. You will have to pay if you wish to continue to take part after the 12-week program. The cost to continue in the program for a 12-week maintanence period will be subsidized; however, the cost may vary among facilities (fee for service). There may be additional costs to you for taking part in this study such as:

- transportation
- parking costs at the YMCA or municipal fitness centres
- meals
- babysitting, etc.

Possible Costs After the Study is Complete

You may not be able to receive the study intervention after your participation in the study is completed. There are several possible reasons for this, some of which are:

- Your caregivers may not feel it is the best option for you;
- You may decide it is too expensive and insurance coverage may not be available;
- The intervention may not be available free of charge.

The principal investigator will discuss these options with you.

WILL I BE COMPENSATED FOR PARTICIPATING IN THIS STUDY?

You will not be paid for taking part in this study. However in the case of research-related side effects or injury, as a direct result of participating in this research, you will receive all medical treatments or services recommended by your doctors.

Although no funds have been set aside to compensate you in the event of injury or illness related to the study treatment or procedures, you do not give up any of your legal rights for compensation by signing this form.

WHAT ARE MY RIGHTS AS A PARTICIPANT IN THIS STUDY?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study. You have the right to be informed of the results of this study once the entire study is complete. If you would like to be informed of these results, please contact the principal investigator.

The results of this study will be available on a clinical registry; refer to the section titled “Where can I find online information about this study?”. Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form you do not give up any of your legal rights against the hospital, investigators, sponsor, involved institutions for compensation or their agents, nor does this form relieve these parties from their legal and professional responsibilities.

IS THERE CONFLICT OF INTEREST RELATED TO THIS STUDY?

There are no conflicts of interest declared between the principal investigator and sponsor of this study.

WHAT IF RESEARCHERS DISCOVER SOMETHING ABOUT ME AS A RESEARCH PARTICIPANT?

During the study, the researchers may learn something about you that they didn't expect. For example, the researchers may find out that you have another medical condition.

If any clinically important information about your health is obtained as a result of your participation in this study, you will be given the opportunity at that time to decide whether you wish to be made aware of that information.

WHERE CAN I FIND ONLINE INFORMATION ABOUT THIS STUDY?

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

The study registration number to use this website is: NCT02984163

WHO DO I CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, or if you suffer a research-related injury, you should talk to the project coordinatior or principal investigator. These person(s) are :

Dr. Christopher Sellar, PhD (Research Coordinator)	780-492-6007
Name	Telephone
Dr. Margaret McNeely, PT,PhD	780-432-8716 or 780-248-1531
Name	Telephone

Dr. Margaret McNeely can also be paged through the Cross Cancer Institute Switchboard at 780-432-8771

If you have questions about your rights as a participant or about ethical issues related to this study and you would like to talk to someone who is not involved in the conduct of the study, please contact the Office of the Health Research Ethics Board of Alberta – Cancer Committee at:

Telephone: 780-423-5727 Toll Free: 1-877-423-5727

SIGNATURES

Part 1 - to be completed by the potential participant.

	Yes	No
Do you understand that you have been asked to take part in a research study?	☐	☐
Do you understand why this study is being done?	☐	☐
Do you understand the potential benefits of taking part in this study?	☐	☐
Do you understand the risks of taking part in this study?	☐	☐
Do you understand what you will be asked to do should you decide to take part in this study?	☐	☐
Do you understand the alternatives to participating in this study?	☐	☐
Do you understand that you are free to leave the study at any time, without out having to give reason and without affecting your future health care?	☐	☐
Do you understand who will see your records, including health information that identifies you?	☐	☐
Do you understand that by signing this consent form you are giving us permission to access your health information if applicable?	☐	☐

Do you understand that by signing this consent form that you do not give up any of your legal rights?	☐	☐
Do you understand that your family doctor/health care provider will/may be informed of your participation in this study?	☐	☐
Have you had enough opportunity to ask questions and discuss this study?	☐	☐

By signing this form I agree, or *allow the person I am responsible for*, to participate in this study.

Signature of Participant /*Substitute Decision-Maker*	PRINTED NAME	Date

(As a Substitute Decision-Maker, you are being asked to provide informed consent on behalf of a person who is unable to provide consent for him/herself. If the participant gains the capacity to consent for him/herself, your consent for them will end.)

Part 2 - to be completed by the principal investigator or designee who conducted the informed consent discussion. Only compete this section if the potential participant has **agreed** to participate.

I believe that the person signing this form understands what is involved in the study and has freely decided to participate.

Signature of Person Conducting the Consent Discussion	PRINTED NAME	Date

Part 3 - to be completed only if the participant is unable to read or requires assistance of an oral translator/interpreter.

- The informed consent form was accurately explained to, and apparently understood by the participant*/substitute decision maker.*
- Informed consent was freely given by *or on behalf of* the participant.

Signature of Impartial Witness/Interpreter	PRINTED NAME	Date

**You will be given a copy of this signed and dated consent form prior to participating in this study.*

Appendix B

Baseline Data Collection Sheets

Fitness Testing Data Sheet

Testing Time Point: Baseline 12-week

Vitals

Resting Heart Rate	**bpm**
Resting Blood Pressure	**mmHg**
Resting O_2 Saturation	**%**

Body Composition

Height (to nearest 0.5 centimeter)	**cm**
Weight (to nearest 0.1 kg)	**kg**
Waist circumference (to nearest 0.5 cm)	**cm**
Hip circumference (to nearest 0.5 cm)	**cm**

Musculoskeletal

Hand Grip	Trial 1	Trial 2
RIGHT	**kg**	**kg**
LEFT	**kg**	**kg**

Flexibility

Shoulder Flexion	Trial 1	Trial 2*
RIGHT	°	°
LEFT	°	°

Sit and Reach (to nearest 0.5cm)	**1)** **cm**	**2)** **cm**

OPTIONAL TESTS

Upper & Lower Body Strength	Bench Press	Leg Press
1 Repetition maximum (lbs)*		
Seat Height:		
Blocking?	Y / N	Y / N

CORE - Plank Test (to nearest 0.1 sec)	

Function

Sit to Stand Test (# of reps in 30 sec)	

Balance

	Standing on RIGHT Leg		Standing on LEFT Leg	
	Trial 1	Trial 2*	Trial 1	Trial 2*
Eyes OPEN (to nearest 0.1 s)	s	- - - - - - - - - -	s	- - - - - - - - - -
Eyes CLOSED (to nearest 0.1 s)	s	s	s	s

*If the participant loses balance during the initial 3 seconds of the Eyes CLOSED trial, a second trial is allowed

6-Minute Walking Test

2-min Heart Rate	bpm
2-min RPE (0-10)	
4-min Heart Rate	bpm
4-min RPE (0-10)	
6-min Heart Rate	bpm
6-min RPE (0-10)	

Lap length (to nearest 0.1m)	m
Number of completed laps	
Partial laps distance (to nearest 0.1m)	m

Did the participant stop before the end of the test? YES / NO

Recovery Heart Rate	**bpm**
Recovery Blood Pressure	**mmHg**
Recovery O_2 Saturation	**%**

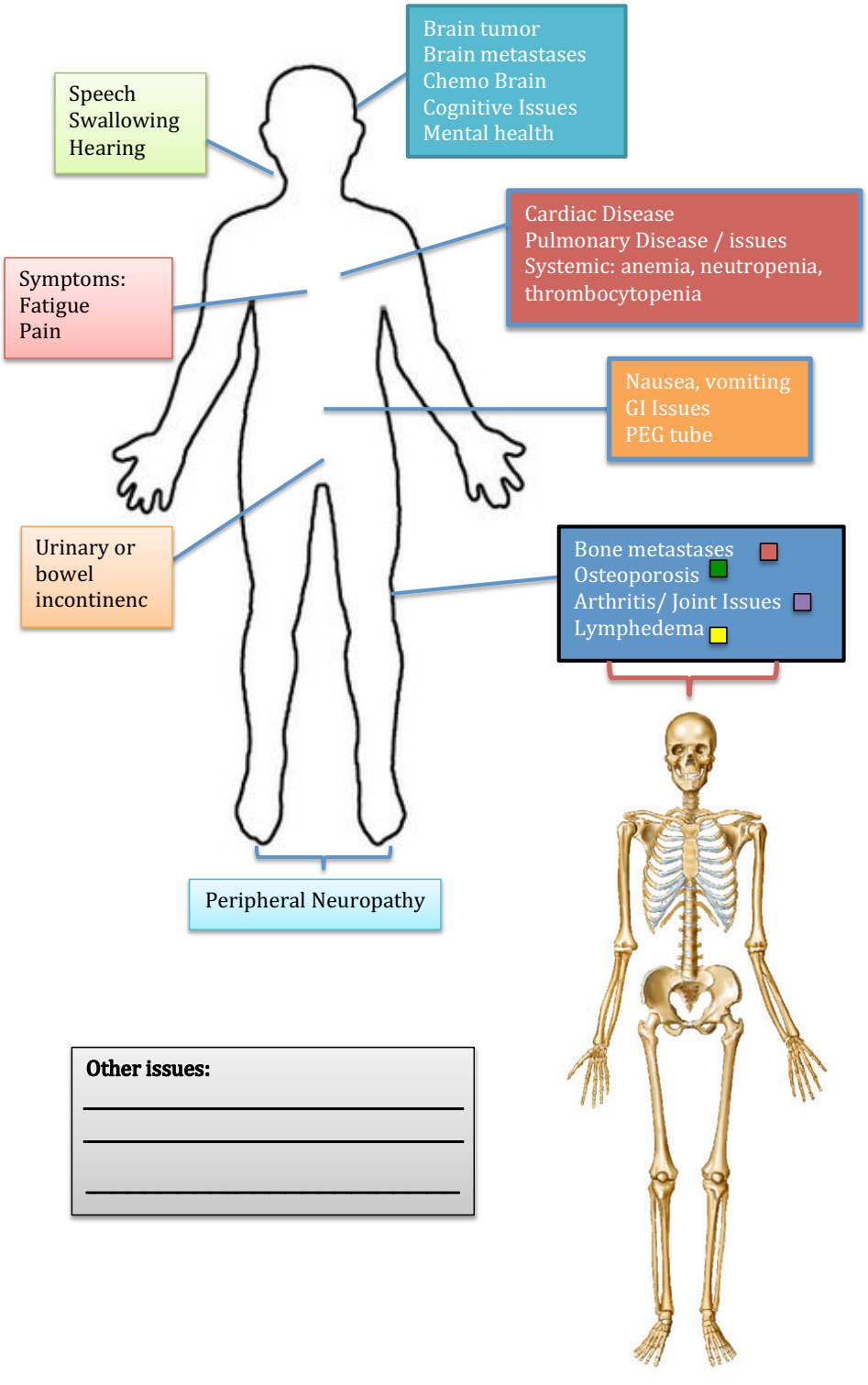
Appendix C

Interview

Interview questions

Question	Answer
What are your main goals for participating in the program?	
What issues are you still concerned about post-cancer treatment?	
What are your concerns with participating in the program?	
What exercises would you like to specifically work on?	
In your previous TrueNTH experience, what exercises do you dislike and why?	
In your previous TrueNTH experience, what exercises do you like and why?	

Body diagram



Appendix D

Six-Minute Walk Test

Six-Minute Walk Test Procedures

1. The participant should sit in a chair at least 10 minutes before the start of the test. During this time, explain to the participant that you will test their aerobic fitness with a walking test, discuss any contraindications, measure blood pressure, pulse and oxygen saturation, ensure safe clothing and shoes, explain the Borg scale
2. Assemble necessary equipment (lap counter, timer clipboard, borg scale, worksheet, pen)
3. Help the participant put on the heart rate monitor. Ensure that it is working properly before starting the test.
4. Instruct the participant to walk the course as fast as possible. Ask the participant to inform you at any point during the test if they feel dizzy, lightheaded, and nauseous, or heaviness, tightness or constricting in the chest, down the arm or into the shoulders or upper back.
5. Measure heart rate and RPE (Borg Scale 6-20) at 2, 4 and 6-minute marks. Record final distance on exercise data form
6. If the participant needed a break during the test, record the reason for the breaks and number of breaks.
7. Have the participant cool down by walking at a light intensity for one minute afterwards.

Appendix E

Sit-to-Stand Test

Sit-to-stand test procedures

1. Explain to the participant they will now be doing a sit to stand test to assess their functional lower body strength.
2. Place a chair with the back against the wall to prevent the chair from sliding. The participant wears shoes for this test.
3. The participant starts in the seated position with arms crossed at their chest. The participant is to be seated in the middle of the chair, back straight, feet shoulder width apart, and arms crossed in front of the chest
4. They will rise to a full stand and then return to a fully seated started position (Their back does not need to touch the back of the chair).
5. The participant will be allowed to practice one or two repetitions before completing the test
6. The participant will complete as many repetitions as they can for 30 seconds. Each time the individual reaches a stand with full hip extension that is counted as a single repetition. They must ensure that they reach a fully upright standing position and that they return to the seated position with their bottom in contact with the chair for the repetition to count.
7. Inform the participant that you will give them a 'ready-set- go' cue to start the test. Ensure that you start your stopwatch simultaneously with 'go'.
8. The tester silently counts the completed of each correct stand. Incorrectly executed stand are not to be counted.
9. The score is the total number of stands within 30 seconds. If the participant is more than halfway up at the end of 30 seconds, it will count as a full stand.

Appendix F

Unipedal Stance Test

Unipedal Stance Test

1. Explain to the participant that you will now test their static balance
2. Ask the participant to remove their shoes prior to beginning the test
3. Give the participant the following background information before starting the test:
    4. Both feet will be tested
    5. They are to stand with their arms crossed over their chest for the duration of the test
    6. Both legs will be tested with eyes open first followed by eyes closed
7. Provide the participant with termination criteria:
    8. Uncrosses or uses arms to maintain balance
    9. Moves the raised foot away from the standing limb or touches the floor with the raised foot
    10. Moves the weight bearing foot to maintain balance
    11. Exceeds maximum duration of 45 seconds
    12. Opens eyes during the eyes closed one leg stance test

Appendix G

One-Repetition Maximum Test

1-RM procedures

1. Explain to the participant that you will now assess their upper and lower body strength using the vertical bench and leg press machines
2. Adjust seat height to ensure proper technique, safety and comfort
3. Explain to participant that you are measuring the maximum weight they can lift one time (for 1RM)
4. Participant starts with a warm up of 5-10 repetitions at a light to moderate load, expected to be close to his 10-RM
5. The participant will be asked to rate the perceived load of the warm-up resistance weight on a scale of 1-5, with 1 = very easy and 5= maximal/ full effort.
6. The load will be increased relative to the participant's response. Once the participant reports a score of 4 (close to maximal effort) out of 5, a small increase in weight will be added and a 1 RM will be attempted.
7. Ample rest (at least 2-5 minutes) will be allowed before each 1 RM attempt.
8. The goal will be to determine the participant's 1 RM or 8RM in a maximum of 3 trials.

Appendix H

Grip Strength

Grip strength procedures

1. Explain to the participant that you will now assess their grip strength, which is a good indicator of overall muscle strength.
2. Adjust the dynamometer so that the second joint of their fingers rests on the handle.
3. Ask the participant to hold the dynamometer in line with their forearm and away from their side (level with their thigh).
4. Explain to the participant not to swing their arm or bend their elbow or wrist during the test, and that neither the dynamometer nor their arm can touch their body or any other object during the test.
5. Tell the participant that they will get two trials per hand, alternating hands after each trial for a combined score of your highest score from each hand.
6. Ask the participant to take a deep breath in and then squeeze as hard as they can while exhaling.
7. Alternate hands, allowing two trials per hand.
8. Ensure the participant is exhaling while squeezing the dynamometer.
9. Ensure the dial is set to zero prior to the next trial
10. Record the reading to the nearest kilogram. Combine the maximum score for each hand on recording sheet.

Appendix I

Height and weight

Height

1. Ask the participant to remove their footwear and any hats and/or scarves.
2. Ask the participant to stand looking straight ahead with their arms hanging at their sides, feet together and their heels and back in contact with the stadiometer. Instruct the participant to stand as tall as possible (with heels remaining in contact with the floor) and take a deep breath.
3. If the participant has thick or a large hairstyle, depress the hair for an accurate measurement.
4. Record the measurement to the nearest 0.1 cm. (Modification from CPAFLA, which is to the nearest 0.5 cm).

Weight

1. The participant's shoes should remain off after the height measurement. Ask participant to remove anything from their pockets, and heavy jewellery, and unnecessary clothing (e.g. Sweatshirt).
2. Ensure that the scale has been accurately calibrated and resting on a hard, flat surface. The scale should read zero when the participant is not standing on the scale.
3. Ask the participant to step on the scale and look straight ahead, with their arms hanging by their sides.
4. Record weight to the nearest 0.1 kg.

Appendix J

Waist and Hip Measurements

Waist Circumference

1. Waist circumference is measured at the top of the iliac crests.
2. Sit in a chair facing the participant.
3. The measurement should be taken on bare skin if the participant is comfortable.

- Ask the participant to roll up their shirt and/or tuck it into their bra to ensure that it is not in the way. NOTE: Do not have the Participant hold their shirt up, as this can affect the accuracy of the measurement.
- If necessary, also ask the participant to lower the waist of their pants slightly to expose the top of their hips.

4. Ask the participant if it is ok to feel for the top of their hip bones and make a mark on both hips with a washable marker.
5. Use your index and middle fingers held horizontally to gently feel for top of the iliac crests. Make a mark with washable marker at the top of each iliac crest.
6. Ensure that the tape measure is level and directly over the marks made on the iliac crests. Pull the tape measure with sufficient tension so that there is no slack, yet without any indentation to the skin. Ask the participant to relax their arms at their sides.
7. Take the measurement at the end of a normal expiration.
8. Record the measurement to the nearest 0.1 cm. (Modification from original source, which is to the nearest 0.5 cm)

Hip Circumference

1. Hip circumference is measured at the greatest gluteal protuberance.
2. Sit in the chair and ask the participant to stand with their feet together and right hip facing you. Ask them to cross their arms at their chest, with hands at the shoulders.
3. Ensure that the tape measure is level and pull the tape measure with sufficient tension so that it is firmly against the clothing.

   Have participant lift long shirts or other bulky fabrics out of measurement area.

Appendix K

Time and Resources

Time and resources for exercise specialist

	Time	Exercise equipment	Additional resources/staff
Personal Training	**Personal Training** Preparation: 30 minutes Exercise supervision: 270 minutes **Week total minutes: 425 minutes**	Mats, dumbbells, exercise ball, bosu ball, exercise bench, treadmill, elliptical machine, stationary bike, ergometer, exercise bands, mini ball, yoga block	Ice and ultrasound machine administration by physiotherapist, one-on-one X 2 participants for shoulder and knee issues.
Circuit Training	**Circuit Training** Preparation: 60 minutes Exercise class: 70 minutes **Week total minutes: 420 minutes**	Mats, dumbbells, exercise ball, bosu ball, exercise bench, stationary bike, exercise bands, mini ball, yoga block	Physiotherapy consult for pelvic floor exercises, modifications for shoulder, hip, knee and low back issues
Total Weekly minutes	**Week 1: 425; Week 2: 420; Week 3-5: 415; Week 6-7: 410; Week 8-9: 400; Week 10-11: 390; Week 12: 385**		

Appendix L

Data Collection Sheet

Exercise sheet

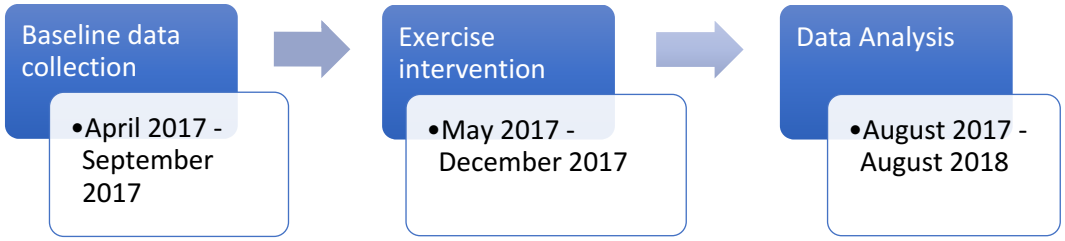
First N											
Warm–up: 3–5 mins of light aerobic exercise (treadmill, walking, bike).											
Exercise Type				Date:		Date:		Date:		Date:	
Aerobic			Type								
			Duration (minutes)	10-15		10-15		15-20		15-20	
			Intensity level								
			RPE	2-3							
Muscle Group	**Machine OR Exercise**	**Exercise Details (machine settings, etc)**		Sets x Repetitions							
				2x10		2x12		3x10		2x10	
				lbs	✓	lbs	✓	lbs	✓	lbs	✓
			Seat Height:								
			Seat Height:								
			Seat Height:								
			Seat Height:								
			Seat Height:								
	Hip Extension/ Glute Press										
			Seat Height:								
	Single Leg Balance (one leg)		Foam + pull band								
Stretch	**Muscle Groups: Hamstrings, Quads, Calves, Pecs, Triceps**										
	2 × 20-30sec										
			RPE								

Rating of Perceived Exertion (RPE) SCALE												
0	0.5	1	2	3	4	5		6	7	8	9	10	·
None	Very, Very	Very Light	Light	Moderate	Somewhat Strong	Strong			Very Strong			Very, Very	Maximal
Trainer Comments/Notes:													

Appendix M

Timeline

Timeline


Baseline data collection
•April 2017 - September 2017
Exercise intervention
•May 2017 - December 2017
Data Analysis
•August 2017 - August 2018

Appendix N

Intensity Calculation

Intensity calculation

(Final 12-week 1RM / baseline 1RM) / 0.60 = adherence percentage