Impact of a 4-Week Home-Based Exercise Program on the Functional Capacity of Advanced Cancer Patients: A feasibility pilot study

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Abstract

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Filareti Patronidis

Research has demonstrated that a physically active lifestyle can counter some of the cardio-respiratory and musculoskeletal losses associated with cancer. Still, exercise guidelines for advanced cancer patients are unspecific, and exercise prescription can be complicated, due to a multitude of factors that may influence the degree of physiological and functional decline from patient to patient. In the present study, twenty-one supportive care patients with stage III or IV cancers were prescribed a 4-week exercise intervention, in conjunction to standard care. The program included 12 unsupervised resistance training and walking sessions, and participants were assessed pre and post exercise intervention. The primary aim of this study is to examine pre-post exercise program changes in function, strength, body composition, energy expenditure, and health-related quality of life (HRQOL). Functional tests, including the 6-minute-walk-test (6MWT) were used to assess performance. Body composition was assessed using dual-energy x-ray absorptiometry (DXA) and accelerometers were used to assess energy expenditure and step-count before and after exercise intervention. The Edmonton Symptom Assessment System (ESAS) and the abridged Patient-Generated Subjective Global Assessment (aPG-SGA) questionnaires were used to examine symptom profile and health related quality of life (HRQOL). We hypothesized improvements in functional scores and increased daily energy expenditures post-exercise as compared to baseline. The secondary aim of the study is to assess its feasibility in the given population. Feasibility was evaluated based on: i) recruitment rate, ii) retention rates, iii) test performance, iv) exercise program tolerability, and v) adherence to prescription. Paired t-tests were used to assess pre-post intervention differences. Findings indicate statistical and clinical significant improvement in 6MWT distance. Pre-post reports of HRQOL were maintained with significant decrease in pain. Upper and lower body strength significantly improved over the 4 weeks. Daily energy expenditure and daily step-count also showed meaningful increase post-exercise intervention. Our findings suggest that, the proposed exercise prescription encourages a more active lifestyle and can improve functionality of supportive care cancer patients.

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List of Abbreviations

6MWT: 6-Minute Walk Test
6MWTD: 6-Minute Walk Test Distance
ACSM: American College of Sports Medicine
aPG-SGA: Abridged-Scored Patient-Generated Subjective Global Assessment
ASA: American Society of Anesthesiologists
ASMI: Appendicular Skeletal Muscle Index
CONSORT: Consolidated Standards of Reporting Trials
CPET: Cardiopulmonary Exercise Test
CRT: Chemo-radiation treatments
CV: Cardiovascular
DNA: deoxyribonucleic acid
EX R_x: Exercise Prescription
DXA: Dual-energy X-ray Absorptiometry
EE: Energy Expenditure
ESAS: Edmonton Symptom Assessment System
FITT: Frequency, Intensity, Time & Type (criteria used to for exercise prescription)
FVC: Forced vital capacity
HGS: Hand Grip Strength
HR_{max}: Maximal heart rate
HR_{peak}: Peak heart rate
HRR: Heart rate reserve
IT: Interval Training
LB: Lower body
MCMD: Minimal clinically meaningful difference
MET: Metabolic Equivalent of Task
MUHC: McGill University Health Centre
MUHC-REB: McGill University Health Centre Research Ethics Board
PA: Physical Activity
WHO: World Health Organization
NCI: National Cancer Institute
HRQOL: Health-Related Quality of life
RCT: Randomized control trial
RM: Repetition maximum
SBP: Systolic blood pressure
SOB: Shortness of breath
UB: Upper body
VO_2: Volume of oxygen consumption
WB: Whole body
xMWT: x-Minute walk test

Chapter I

Introduction

Cancer

Cancer and Projected Statistics in Canada

Cancer is the second leading cause of death worldwide, accounting for every 1 in 6 deaths globally in 2018 (WHO, 2018). In Canada, cancer is the primary cause of death for 1 in 4 Canadians (Canadian Cancer Statistics, 2018). Projected statistics report that the four most commonly diagnosed cancers will remain the same, and include: lung, breast, colorectal, and prostate cancers (WHO, 2018). Together, these four major cancers will encompass half of newly diagnosed cancers by 2030, and will primarily affect the senior population (Canadian Cancer Statistics, 2018). Closely followed by colorectal cancers, prostate cancer will be the most commonly diagnosed cancer as Canadian men age, with a survival rate of five years. Fortunately, cancer survival rates have generally improved in the last few decades, and continue to improve due to new advancements in technologies, screening processes, and treatments. Improvements in cancer management are also reflected in that the incidence rate for all cancers combined is expected to remain steady in the coming years (Canadian Cancer Statistics, 2018).

Nevertheless, according to recent statistic publications by the Canadian Cancer Society Statistics Report (2018), 1 in 2 Canadians will be diagnosed with cancer at some point in their lifetime, and only half are expected to survive (*See Appendix A*). Moreover, the total number of Canadians diagnosed with cancer is on the rise. The reported long-term projections, estimate that number of cancers diagnosed in 2030 will be increased by 80% as compared to 2005 (Canadian Cancer Statistics, 2018). This dramatic increase is partly due to the fact that Canadians are growing older as a population. In fact, by the year 2030, the number of adults aged 65 and over will have doubled, jumping from a ratio of 1 in 8 to 1 in 4. Canada's population is also increasing in number, and is expected to welcome another 10 million people by 2030 (Canadian Cancer Statistics, 2018). These increases in population size and age will challenge Canada's health care system, and the surge in cancer cases may push it to capacity. In consequence, there is urgent need for improved, feasible, and effective cancer management plans.

Introduction to Cancer & Pathophysiology Overview

Cancer is an umbrella term used to describe a group of related diseases. In all cancers, some of the body's cells will start to divide abnormally without stopping (NCI, 2015). Normally, cells follow an orderly cycle of life and death. New cells mature, and when they become old, damaged, or abnormal, they die, and new ones replace them. Contrastingly, in the case of cancers, when abnormal or dysplastic cells develop, they continue to survive and multiply in an uncontrolled fashion called hyperplasia (NCI, 2015). Cancer cells are different from normal cells, because they lack specific function and can continue to grow where they are not needed, ignoring normal cues for apoptosis. These extra cells continue to divide and proliferate, and may collect to form a cancerous tumor (NCI, 2015).

Essentially, tumors are classified in one of two categories: benign or malignant. Some tumors are considered benign, which means that are incapable of spreading and typically will not cause harm, unless they grow large, and compress other important structures like vital organs. Benign tumors can be removed surgically and usually do not grow back. In contrast, cancerous tumors are considered malignant, meaning that they are capable of spreading and invading other tissues, and even if they are surgically removed, run the risk of growing back (NCI, 2015). With cancerous tumors, metastasis of cancer cells is possible through the blood or lymphatic system to reach other areas in the body, away from the original tumor site. Furthermore, cancerous tumors can suppress the immune system, and can control certain immune cells to protect the tumor from immune system attack. Similarly, cancer cells may relinquish control of normal cells to feed and supply the tumor. For example, cancer cells will use normal cells to build blood vessels for the tumor, so it can absorb nutrients and oxygen and expel waste like healthy body tissues do (NCI, 2015).

Cancer Classification

Classifications of both benign and malignant tumors are based on the type of cell they arise from. The majority of cancers will fall into one of the following classes: carcinomas, sarcomas, leukemia, lymphomas, myelomas, or central nervous system cancers (Cooper, 2000). Carcinomas, which represent 90% of human cancers, originate in epithelial cells, which line the body's inner organs, cavities and outer skin. Appearing more rarely, sarcomas will originate in connective tissues like bones, cartilage, muscles and tendons (Cooper, 2000). Leukemia,

lymphomas, and myelomas will originate in the bone marrow, the lymphatic system, and the immune system, respectively. Lastly, cancers originating in the brain or spinal cord are known as central nervous system cancers (Cancer Research UK, 2017). Cancers are also named based on the body part they originate in, like breast or lung carcinomas, for example. Even when cancer metastasizes, it is named after the primary cancer site (Cooper, 2000). For instance, if breast cancer metastasized to the lung, it is called metastatic breast cancer to the lung and not lung cancer (Canadian Cancer Society, 2018).

Cancer Staging

A pathology test is usually necessary to identify and grade a cancer. This involves a biopsy of the tumor that is then examined under the microscope for presence of malignancy, type and stage of cancer (Quebec Cancer Foundation, 2017). Typically, cancers are staged using the "T-N-M" grading system (Canadian Cancer Society, 2018) *(See Appendix B)*. This globally recognized grading system is broken down into 3 key criteria, where 'T' is for tumor size, 'N' is for number of lymphatic nodes affected and 'M' is for metastasis. Tumor size refers to the primary cancer tumor and it's invasion to local tissues if any. To stage the size of the tumor, 'T' is followed by a number from 1 (smallest) to 4 (largest). Similarly, the number of nodes affected is denoted as 'N' followed by a number from 0 (least extension) to 3 (most extension). In turn, 'M' will be followed by either 0 (absent) or 1 (present), indicating presence or absence of metastasis. In some cases, lowercase letters are used to further specify the degree of metastasis (Canadian Cancer Society, 2018). Other times, cancer may be difficult to stage, for example, if cancer is advanced and history of primary tumor is unknown. In the case of brain cancers, grading will be different, because brain cancer will not metastasize beyond the central nervous system (Quebec Cancer Foundation, 2017).

Epidemiology and Risk Factors

Pathophysiological mechanisms for cancer are attributed to various causes. Established causes include genetic material being mutated by errors in replication or repair processes, exposure to various environmental factors and carcinogens, or through certain viruses (e.g. Epstein-Barr virus, hepatitis B and C, human papillomavirus) (Cooper, 2000 ; Arem et al. 2018). Genetic changes evoking cancer include alterations in 3 main types of genes: proto-oncogenes,

tumor-suppressor genes, and DNA repair genes (NCI, 2015). Changes in proto-oncogenes, which are responsible for normal cell division and growth, solicit development of oncogenes, which enable cells to live passed their expiration date and multiply uncontrollably (NCI, 2015). Similarly, tumor-suppressor genes also control proper growth and division of cells. Therefore, alterations in tumor-suppressor genes will also enable uncontrolled growth and division of cells. Lastly, DNA repair genes, which are responsible for mending damaged cells, may present with mutations. In consequence, mutated cells in DNA repair genes can transfer mutations onto other genes, and together these mutations can create cancerous cells (NCI, 2015). Molecular research finds that certain mutations correlate with certain cancers. Thus, cancers are also commonly characterized by the gene alterations that seem to be driving them regardless of where they appear in the body or how cancer cells appear under the microscope (NCI, 2015).

Besides non-modifiable genetic alterations, there exist many modifiable risk factors to cancers that we can control through improved lifestyles. According to a recent review by Arem and Loftfield (2018), up to half of incident cancers appear to be caused by modifiable risk factors. Lifestyle choices like eliminating tobacco use, using sunscreen, moderating alcohol consumption, and being physically active, may significantly reduce risk of cancer (Arem et al. 2018).

Supportive Care Treatments for Advanced Cancers

For advanced cancer patients, aggressive chemo-radiotherapy treatments (CRT) are most often required for a chance to survival. Chemo-radiotherapy treatments are an integral part of cancer management and are prescribed to cancer patients in order to kill cancer cells, downsize cancerous tumors, improve operability and decrease likeliness of cancer recurrence (Andre et al., 2009; Vicini et al., 2002; Burris, 1997). Despite its effectiveness against cancer cells, CRT has a very high toxicity profile for the whole body, and is deleterious for many non-cancerous, healthy cells (West et al., 2014; Cancer Research UK, 2005). Consequently, advanced cancer patients undergoing CRT are often impacted by decreases in muscle tone and cardio-respiratory fitness, as well as, significant increases in fatigue level and weakness (West et al., 2014; Gilliam et al., 2011; Van Norren et al., 2009; Carvalho et al., 2009; Chen et al., 2007). Sometimes, cancer treatments may also inflict cognitive deficiencies like declines in attention, memory and executive functioning (Vichaya et al., 2015). For patients undergoing curative surgery (surgical

removal of tumor) in addition to receiving CRT treatments, physical and functional decline are always expected, and even more so, for patients who are deconditioned before surgery. Deconditioned patients will also have an increased risk of surgical complications (Christensen, 1993).

Cancer & Treatment-Related Declines

Fatigue is by far, the most debilitating symptom reported by cancer patients. Fatigue is also the number one anticipated side-effect even before patients start receiving treatments, according to the large scale Rochester Cancer Center Community Clinical Oncology Program study, which included 938 patients (Hoffman et al., 2004). Even without treatments, cancer-related fatigue is widely reported by patients upon cancer diagnosis and persists post-treatment for many survivors (Hoffman et al., 2007). Cancer related fatigue is not the same as 'regular' fatigue or drowsiness experienced by healthy individuals, as it is not relieved by rest or sleep (Hoffman et al., 2007). Unsurprisingly, exposing the already chronically fatigued body to aggressive CRT treatments only amplifies the degree of fatigue experienced by supportive care patients. Research indicates that up to 80% of patients undergoing chemotherapy and up to 90% of patients undergoing radiation therapy experience fatigue (Hoffman et al., 2007; Curran et al., 2004; Schwartz et al., 2000).

The onset of fatigue in cancer patients contributes to decreased physical and functional capacities. The mechanism of physical fitness decline due to CRT is not fully understood. However, it is known that oxidative damage from chemotherapy can cause an up-regulation of ubiquitin-ligase (an enzyme that signals the degradation of proteins), an increase mitochondrial death, and important losses in muscle mass (Buttke et al., 1994). Other known mechanisms include interactions with oxygen to produce reactive oxygen species (ROS) (Chen et al., 2007), while others include decreased antioxidant levels. In sum, although mechanisms remain obscure, many chemotherapeutic agents affect cardio-respiratory and microcirculatory function, as well as, mitochondrial and cellular metabolism. Consequently, these mechanisms lead to increased fatigue, especially in advanced cancer patients, and even more so in patients with cachexia (muscle wasting syndrome), who can lose up to 75% of their skeletal muscle mass (Preston et al., 1987). Such losses in muscle mass result in increased fatigue, decreased quality of life, and increased mortality (Tisdale, 2001).

Radiation therapy has also been associated to tissue fibrosis (Renzi et al., 1992) and arteriosclerosis (Rubin et al., 1992). When chemotherapy and radiotherapy treatments are combined, the negative effects on cardiovascular and muscular systems are amplified (Bezwada et al., 1998), sometimes resulting in left ventricular function impairments, abnormal pressure and volume relationships and decreased ejection fraction (d'Avella et al., 1998). Depending on the specific type of anti-cancer treatment, side effects may including anemia, appetite loss, nausea, hair loss, diarrhoea, hand-foot syndrome, cardiotoxicity and haematological toxicity (Rubin et al., 1992 ; d'Avella et al., 1998). Moreover, a study by Woo et al. (1998) showed that cancer survivors having undergone both chemotherapy and radiotherapy experienced higher levels of fatigue and showed lower functional capacity scores than their counterparts who had received one of the treatments exclusively.

Recent studies have quantified the impact of CRT on cardio-respiratory fitness in cancer patients. Findings from cardiopulmonary exercise testing (CPET) indicate that oxygen uptakes (VO_2) at ventilatory threshold and peak exercise (VO_{2peak}) were significantly reduced (Fresard et al., 2013; Jack et al., 2016; Sinclair et al., 2014; Yeh et al., 2004). In fact, it has been suggested that 12 weeks of chemotherapy is equivalent to an entire decade of physical decline in terms of cardio-respiratory fitness (Lakoski et al., 2012). The decline in red blood cells, hemoglobin, and overall decline in cardio-respiratory fitness attributed by chemotherapy treatments, in conjunction with tissue fibrosis (often seen in lungs) and, at times, cardiac abnormalities attributed by radiation therapy, increases risks of cardiovascular disease mortality and mortality in general (Yeh et al., 2004, Darby et al., 2003; Huddart et al., 2003) . Naturally, factoring in sedentary behavior -which is often seen in cancer patients-, adds to the heavy burden on the cardio-respiratory system (Lakoski et al., 2012). Decreases in physical activity (PA) due cancer-related fatigue, depression or lack of motivation may result in reduced muscle and bone mass, decreased strength, endurance, heightened symptoms and increased pain. Consequently, patients experience decreases in functionality as they struggle to execute activities of daily living, increase their dependency and experience poorer HRQOL (Vogelzang et al., 1997).

Increased physical decline is also a reality for patients undergoing curative surgery. Firstly, decline in cardio-respiratory fitness associated to pre-operative CRT treatments increase risks of surgical complications (West et al., 2015). Close to one-third of patients undergoing major colorectal re-sectioning surgery experience painful post-operative complications (Schilling

et al., 2008) including wound infection, gastrointestinal infection, and motility complications like ileum and bowel obstruction (Tevis et al., 2016). Even in the absence of complications, major surgeries are associated to a 40% reduction in physiologic and functional capacities (Christensen et al., 1993).

The table below, published by Kleckner et al. (2018), summarizes the most prevalent toxicities attributed to cancer and its treatments. Toxicities listed in this abridged table appear in order of high priority, identified by the National Community Oncology Research Program (NCI-NCORP, 2015).

Table 1: High priority toxicities from cancer and its treatments

Toxicity	Definition	Prevalence
Fatigue	Distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent physical activity and interferes with usual functioning (Berger et al., 2010)	• Approximately 80–100% of patients with cancer (Stone et al. 2000) • Approximately 25–33% of cancer survivors up to 10 years after diagnosis (Carson et al., 2009; Bower et al., 2012)
Cardiotoxicity	Damage to the heart, leading to chest pain, shortness of breath, heart attack, and heart failure. Cardiotoxicities include cardiomyopathy, myocarditis, pericarditis, acute coronary syndromes, and congestive heart failure (National Comprehensive Cancer Network, 2017)	• Approximately 27% of patients receiving the HER2-inhibitor trastuzumab • Approximately 20–50% of patients receiving inhibitors of VEGFA • Approximately 7% of patients receiving tyrosine kinase inhibitors • Risk is elevated from chest radiotherapy (Moslehi, 2016)
Pain	An unpleasant sensory and emotional experience associated with actual or potential tissue damage (IASP, 2004)	Approximately 59% of patients with cancer (Chang et al., 2000)
Cognitive impairment	Impaired learning, memory, attention, and speed of information processing (Dietrich et al., 2008)	• Up to 75% of patients with cancer and cancer survivors (Janelsins et al., 2011)
Neurotoxicity	Damage to nerve cells in the brain, spinal cord, or periphery (Dietrich et al., 2008) Peripheral neuropathy can cause pain, numbness, tingling, cramping, motor problems, balance impairment, and sexual dysfunction (Postma et al., 2005)	• Up to 68% of patients 1 month after completing neurotoxic chemotherapy • Up to 30% of patients 6 months after completion of neurotoxic chemotherapy (Seretny et al., 2004)

This list only includes highest priority toxicities determined by the National Cancer Institute (NCI) Community Oncology Research Program (NCORP) Symptom Management Committee.HER2 = human epidermal growth factor receptor 2; VEGFA = vascular endothelial growth factor A; IASP= International Association for the Study of Pain. Refer to Kleckner et al. (2018) for complete table.

Cancer Cachexia

Cachexia, which is characterized by generalized weight loss and muscle wasting, often occurs in consequence of advanced cancers and other chronic disorders. Cancer cachexia is most prevalent in gastrointestinal, pancreatic, lung and colorectal cancers (Dodson et al., 2011). According to a consensus conference for physicians, which took place in Washington in 2008, the clinical definition of cachexia is as follows:

> "Cachexia is a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass. The prominent clinical feature of cachexia is weight loss in adults. Anorexia, inflammation, insulin resistance and increased muscle protein breakdown are frequently associated with cachexia. Cachexia is distinct from starvation, age-related loss of muscle mass, primary depression, malabsorption and hyperthyroidism and is associated with increased morbidity."
> (Evans et al., 2008)

Due to the heterogeneous features of cancer cachexia, its identification poses challenge to clinical practitioners, and only recently, has there been development of a cancer-cachexia classification system using specific clinical criteria (Vigano et al., 2016). The defined classification system includes four different cachexia stages: non-cachexia, pre-cachexia, cachexia, and refractory cachexia. Each stage is defined according to the following five criteria: abnormal biochemistry (A), decreased food intake (B), moderate weight loss (C), significant weight loss (D), and decreased activities and functioning (G) *(see Appendix C)*.

The Role of Exercise

Recent findings demonstrate that patients who adopt a physically active lifestyle while receiving treatments are able to counter some of the cardio-respiratory losses attributed by CRT. Consequently, physically active cancer patients report less depression and a better HRQOL (Mishra et al., 2012; Burke et al., 2013; Cheville et al., 2013; Furmaniak et al., 2016; Brunet et al., 2017; Hsieh et al., 2008).

For patients undergoing surgery, 'prehabilitation', or pre-operative exercise intervention, is emerging in the oncology field as a relevant tactic to increase pre-operative functional reserve (Le Roy et al., 2016). Recent research stipulates, that better results in pre-operative $VO_{2peak,}$ 6-minute walk, and anaerobic threshold tests, predict reduced risk of post-surgical morbidities (Hennis et al., 2011). Prehabilitation exercise programs can also prevent fatigue and physical declines associated to pre-operative CRT treatments (Le Roy et al., 2016).

For patients undergoing CRT treatments, some exercise programs have successfully reversed the deconditioning process attributed by anti-cancer treatments (Courneya et al. 2007; Segal et al., 2009). For example, Courneya et al. (2007) used aerobic training to halt VO_{2peak} decline in breast cancer patients receiving chemotherapy. Similarly, Segal et al. (2009) counteracted cardio-respiratory declines using an aerobic and resistance exercise program in prostate cancer patients receiving radiotherapy. Remarkably, one breast cancer study was successful in achieving an overall increase in cardio-respiratory fitness (11.8% increase over intervention period) using aerobic interval training (Jones et al., 2011). Strength and endurance training programs also help reduce cancer-related fatigue and are recommended to all patients experiencing fatigue (Dimeo et al., 2001; Schmitz et al., 2010). Moreover, PA has been associated with reduced occurrence and recurrence of several cancers (Irwin et al., 2008; Holmes et al., 2005; Holick et al., 2008). Namely, study results suggest that post-diagnosis PA can reduce breast cancer deaths by 34 %, all-cause mortality by 41 % and disease recurrence by 24 % (Ibrahim et al., 2011). In colon cancers, moderate levels of PA have also been associated with a lower risk of death in (Meyerhardt et al, 2006).

Exercise in Cancer Rehabilitation

Physical activity during cancer treatment has delivered some promising results. Numerous studies have illustrated exercise can correct and prevent some of the compromising effects of cancer treatments like fatigue and decreased functionality. The following tables summarize some of these studies (*See Tables 1 & 2 below*).

Table 2: Literature Review of Exercise Interventions Studies in Supportive Cancer Patients

Researchers (Year)	Participant characteristics	Exercise type	Length and Frequency	Intensity	Outcome measure Results
Winningham et al. (1988) & (1989)	Female, 45-48 yrs old Breast Cancer, stage II (n=42 in1988) (n=24 in 1989)	CV: IT cycling	12 weeks, 3x/week, 20-30 mins/session	60-80% HRmax	↔ Arm circumference ↑Lean body mass ↓nausea, ↓body fat
Macvicar et al. (1989)	Female Breast Cancer, stage II (n=45) 43-46 yrs old	CV; IT cycling	10 weeks 3x/week	60-85% HRmax	↓Skinfold sites ↑42% VO_{2peak}
Schwartz et al. (2000) & (2001)	Female Breast Cancer (n=27 in 2000) (n=72 in 2001)	CV: Self-paced walking Home-based	2000:8 weeks 4x/week 35 mins/session 2001: 3 chemo cycles ~9-10 wks, 15-30mins, 3-4days/wk	Self-paced with accelerometers to grade exercise intensity (based on calories expended)	2000:↑10.4% 12MWT ↓Fatigue 2001:↑15% 12MWT
Segal et al. (2001)	Female Breast Cancer Stages I and II (n=123) Age ~51.4 yrs	CV: Walking (supervised vs. unsupervised vs. control) (self report)	26 weeks 5x/week	50-60% VO_{2max}	↓Emotional distress ↑Physical functioning ↔VO_{2max} Unsupervised reported larger change in function when compared to control than supervised.
Segal et al. (2003)	Male Prostate Cancer Age~68.2 yrs (n =155) Androgen deprivation therapy	Resistance	12 weeks 3x/week 2 sets, 12 reps	60-70% 1-RM	↑42% UB strength ↑36% LB strength ↓5% resting SBP ↑HRQOL
Kolden et al. (2002)	Female Breast Cancer stage I and II 45-76 yrs old (n=40)	CV: walking, cycling, stepping Resistance, Flexibility	16 weeks 3x/week	Unspecified	↑34.5% UB strength ↑37% LB strength ↑15.4% VO_{2max} ↑11% flexibility
Adamsen et al. (2003)	Male, Female Leukemia, breast, colon, ovary, testi, cervix, Hodgekins and non-Hodgekins lymph cancers (n=23) 18-63 yrs old	Resistance, CV: cycling, Relaxation	6 weeks 4x/week 3 sets, 5-8 reps	60-100% HRmax 85-95% 1-RM	↑32.5% WB strength ↑ 16 % VO_{2max} ↔ HRQOL

Table 3: Literature review of exercise intervention studies in cancer patients taking place over 4 weeks or less

Researchers (Year)	Participant characteristics	Exercise type	Length and Frequency	Intensity	Outcome measure Results
Dimeo et al. (2008)	Male and Female Cancer patients with mild to severe persistent fatigue after treatment (n=32) Berlin, Germany	CV: treadmill Resistance & Coordination: exercises for major muscle groups	3 weeks ~10 sessions	30 min on treadmill walking	↑physical performance ↓ mental and physical fatigue ↔ depression, anxiety or cognitive fatigue
Li et al. (2012)	Male and Female Patients with colorectal cancer undergoing surgery (n=42) Montreal, Canada	CV & Resistance & Nutrition and anxiety reduction	4 weeks 3x/week (presurgical intervention; outcome measures assessed 4 and 8 weeks post surgery)	30 mins walking moderate intensity and 30mins of resistance training	↑walking capacity and recovery speed of experimental group compared to poor functionality/recovery of control
Gillis et al. (2014)	Male and Female Patients undergoing colorectal surgery (n=77) Montreal, Canada	Home-based program CV & Resistance With nutrition counseling, protein supplements and relaxation exercises	4 weeks, 3x/week (pre-operative or immediately post surgery) and continued for 8 weeks post surgery	50 mins/session 5-min warm-up, 20 min of aerobic exercise (starting at 40%HRR), 20 min of resistance training (8 exercises for major muscle at 8 to 12 repetitions maximum), 5-min cool-down	↑6MWT Distance Meaningful changes in postoperative functional exercise capacity achieved with 4 week prehabilitation
Do et al. (2015)	Female Breast cancer patients who completed chemotherapy (n=62)	Stretching, CV & Resistance	4-weeks post-operative	80 mins/session warm up (10 min), strength (10 min), aerobic (40 min), core stability (10 min), cool down (10 min)	↓fatigue, pain, nausea, and dyspnea ↑HRQOL
Dunne et al. (2016)	Male and Female Patients undergoing elective liver resection for colorectal liver metastases (n=34)	CV	4-weeks 3x/week	5 min warm-up & cool-down, 30 min interval training mod-vigorous on cycle ergometer	↑preoperative VO_2 at anaerobic threshold and peak exercise seen with CPET ↑HRQOL

CV=cardiovascular, CPET= cardiopulmonary exercise test, HRQOL= health related quality of life, 6MWT=6minute walk test, IT=interval training, UB, LB, WB= upper/lower/whole body.

*See full list of abbreviations on page iii

Discussion of literary review

In general, findings indicate positive physical and psychological outcomes through exercise intervention. As seen in Table 2, many of the earlier exercise intervention studies have focused on early stage breast cancer patients (Winingham et al., 1988 & 1989 ; Macvicar et al., 1989; Schwartz et al., 2000 & 2001), but more recent studies have included a wider array of cancer patients (Adamsen et al., 2003; Dimeo et al., 2008). Also, many of the earlier studies focused on aerobic training (Winingham et al., 1988 & 1989; Macvicar et al., 1989; Schwartz et al., 2000 & 2001) rather than resistance training or mixed programs. In contrast, more recent works presented in **Tables 2 and 3**, include mixed training programs incorporating aerobic, resistance and flexibility into exercise sessions (Gillos et al., 2014; Do et al., 2015; Dimeo et al., 2008). Exercise program length, frequency, and, intensity values also varied significantly from study to study, making it difficult to pinpoint the best guidelines for exercise prescription in this population. A closer look reveals that most exercise interventions prescribed 'moderate' intensity exercise or created personalized goals for patients according to their baseline fitness assessments. However, there is a general lack of instruction regarding specific exercises used for resistance training intervention. Listed in Table 3 are studies that include shorter exercise intervention of 4 weeks or less. Interestingly, though these interventions are quite short, they still produced significant improvements in functional and cognitive measures. However, there is still a lack of studies examining advanced cancers in supportive care, and shorter interventions mainly focus on preparation and response to surgery (Gillis et al., 2014; Li et al., 2012). Moreover, there have been no short-term studies (≤4 weeks) examining changes in body composition, strength, and EE before and after exercise for advanced supportive care patients. Also, the use of objective tools, such as, DXA for tracking changes in body composition (reference standard), just as, the use of accelerometers for tracking PA, have not been reported in short-term, supported care studies to date. Thus, further research is required to investigate changes attributed by short-term exercise interventions. Moreover, screening for cancer cachexia is not something that is discussed by any of the aforementioned studies, and its importance will be addressed in the next chapter. Overall, more research is required on the aforementioned fronts, and the following study attempts to address these gaps in literature.

Project overview

Standard care for advanced cancer patients consists of the administration of pharmaceutical treatments, and regular follow-ups by various health care professionals including physicians, physiotherapists, and nutritionists. Despite findings that exercise programs offer significant benefits to advanced cancer patients, professional kinesiologist consultations are not yet offered to patients as part of standard care services. Moreover, exercise guidelines for advanced cancer populations are still very unspecific and exercise prescription can be challenging, due to a multitude of factors that may influence the degree of physiological and functional decline from patient to patient. Few studies have examined both functional performance and physiological changes after brief (4-week) exercise intervention, along with, changes in daily energy expenditure in a group of patients. The objective of this study is to assess the feasibility of a 4-week, home-based exercise program prescribed to patients receiving supportive care at McGill University Health Center's (MUHC) cancer clinic. More specifically, inclusion criteria qualified patients with stage 3 or 4 cancers, receiving anti-cancer treatments, and without cachexia according to the criteria defined in Appendix C (Vigano et al., 2016). All study participants (N=21) received consultation with a kinesiologist and were prescribed exercise intervention for 4 weeks in addition to their standard care. To measure changes in performance, the study called for a pre-post intervention design with the 6MWT as primary outcome measure. Tests included in the Short Physical Performance Battery were secondary measures in assessing performance. Body composition was assessed using dual-energy x-ray absorptiometry (DXA) and accelerometers were used to assess energy expenditure and step-count before and after exercise intervention. Gains in strength were quantified in regards to progression in Theraband™ resistance. We hypothesized improvements in all functional scores, overall body strength, and increased daily energy expenditures post-exercise as compared to baseline. Paired t-tests were used to assess pre-post exercise differences. Feasibility was evaluated based on: i) recruitment rate, ii) retention rates, iii) test performance, iv) exercise program tolerability and v) adherence.

Chapter II

Impact of a 4-Week Home-Based Exercise Program on the Functional Capacity of Advanced Cancer Patients: A feasibility pilot study

Filareti Patronidis, Popi Kasvis, Leonard Rosenthall, Antonio Vigano and Robert Kilgour

Contribution of Authors

Filareti Patronidis: Data collection, recruitment, preparation of manuscript, development of training program, provided original draft to manuscript
Popi Kasvis: Editing of manuscript, assisted in patient recruitment
Leonard Rosenthall: Development of the experimental design and statistical analysis
Antonio Vigano: Co-supervisor, editing of manuscript, assisted in patient recruitment, experimental design
Robert Kilgour: Co-supervisor, development of experimental design, project development, assisted in protocol, preparation and editing of manuscript

Abstract

Introduction: Few studies have examined both functional performance and physiological changes after brief (4-week) exercise intervention, along with, objective changes in daily energy expenditure in a group of patients. The current study investigates the impact of a 4-week, unsupervised, exercise program in stage 3 and 4 cancer patients with a variety of malignancies undergoing supportive care. The primary aim was is to examine pre-post interventional changes in function, body composition, energy expenditure, and health-related quality of life (HRQOL). The secondary aim of this study was to assess its feasibility. Feasibility was evaluated based on: i) recruitment rate, ii) retention rates, iii) test performance, iv) exercise program tolerability and v) adherence.

Methods: All participants (N=21) took part in a prescribed home-based exercise program, which included 12 unsupervised training sessions over a 4-week period. Study design compared pre-post intervention outcome measures. Each training session included self-paced walking, Theraband™ resistance exercises of the upper and lower body, combined with balance and flexibility exercises. Participants were asked to keep record of each session in a provided logbook. Our primary outcome measure for functional performance was the 6-minute-walk test. In addition to traditional functional tests, body composition was assessed using reference standard, DXA, and accelerometers were used to objectively assess energy expenditure and step-count before and after exercise intervention. Lastly, the Edmonton Symptom Assessment System (ESAS) and the abridged Patient-Generated Subjective Global Assessment (aPG-SGA) questionnaires were used to examine symptom profile and HRQOL. We compared all pre-post exercise group means using paired t-tests.

Results: Results of primary outcome measure showed statistical and clinical improvement in the 6MWTD of +44.2 ± 38.0 ($\bar{x} \pm$ SD) between pre and post-intervention assessments. Total SPPB scores were also significantly improved post intervention, primarily due to significant improvement in sit-to-stand time (p=0.025). Lean body mass also showed a trending increase (p=0.066), while fat mass and bone mineral compositions were maintained. Significant increases in end intervention energy expenditures and step count (p=0.01 for both) showed positive behaviour modification and increased PA. There was an improvement in overall body strength as evidenced by the significant increase in elastic resistance in the chest press, seated row, and bicep curl over the 4-week period. Symptom profiles and HRQOL remained generally consistent

throughout the study. To verify feasibility we calculated a retention rate of 75%, recruitment rate of 29%, and adherence rate of 85%. Because these figures are comparable to those of other cancer-exercise studies, a future randomized control trial is feasible.
Conclusion: Our findings imply that the current exercise prescription is beneficial to, and well tolerated by, advanced cancer patients undergoing supportive care. Comparisons between pre-post intervention outcome measures revealed promising improvements in functionality, walking capacity, overall muscle strength, and increased PA.

Keywords: Cancer rehabilitation, exercise, 6MWT, resistance training, energy expenditure, supportive care.

Introduction

Chemo-radiotherapy treatments (CRT) are an integral part of cancer management and are prescribed to cancer patients in order to kill cancer cells, downsize cancerous tumors, improve operability and decrease likeliness of cancer recurrence (Andre et al., 2009; Vicini et al., 2002; Burris, 1997). Despite its effectiveness against cancer cells, CRT has a very high toxicity profile for the whole body, and is also deleterious to healthy cells (West et al., 2014; Cancer Research UK, 2005). Consequently, patients undergoing CRT are often impacted by decreases in muscle mass and cardio-respiratory fitness, as well as, significant increases in fatigue level (West et al., 2014; Gilliam et al., 2011; Van Norren et al., 2009; Carvalho et al., 2009; Chen et al., 2007). One study suggests that 12 weeks of chemotherapy is comparable to an entire decade of cardio-respiratory aging (Lakoski et al., 2012). However, several exercise interventions have successfully reversed the deconditioning process attributed by anti-cancer treatments, validating the important role of exercise in cancer rehabilitation.

In general, previous findings demonstrate better functionality, symptom management, and HRQOL with exercise intervention (Courneya et al., 2007; Segal et al., 2009, Mishra et al 2012; Burke et al., 2013; Cheville et al., 2013; Furmaniak et al., 2016; Brunet et al., 2017; Hsieh et al., 2008). Despite findings that exercise programs offer significant benefits to advanced cancer patients, professional kinesiologist consultations are not yet offered to patients as part of standard care services. Moreover, exercise guidelines for advanced cancer populations are still very unspecific and exercise prescription can be challenging, due to a multitude of factors that may influence the degree of physiological and functional decline from patient to patient. Currently, ACSM guidelines for exercise prescription in cancer population are loosely defined, and justly declare that "appropriate FITT recommendations will vary across cancer experience and requires individualization of Ex R_x" and, that "exercise tolerance may be highly variable during active treatment" (ACSM, 2013).

One important factor that may influence how a patient will receive, and benefit from, exercise prescription is the presence and degree of cancer cachexia (ACSM, 2013). Cancer cachexia is associated with up to 75% loss of muscle mass in refractory cases (Preston et al., 1987) and is described as a "complex metabolic syndrome associated with underlying illness" (Evans et al., 2008). To date, studies have shown that muscular strength and exercise capacity are reduced during cancer cachexia (Stephans et al., 2012; Moses et al., 2004; Baltgalvis et al.,

2010), suggesting that cachectic patients might respond to exercise differently, that they are more deconditioned, and that they might have different needs compared to other cancer patients (Hardee et al., 2017). However, current publications concerning exercise intervention fail to screen for cancer cachexia, and more research is required to evaluate the needs, tolerance and response to exercise for advanced cancer patients with versus without cancer cachexia.

In this study, only patients, without cachexia, receiving supportive care were eligible to participate. The primary aim of this study is to examine pre-post interventional changes in function, strength, body composition, energy expenditure, and HRQOL. Our primary outcome measure for functional performance was the 6-minute-walk test, which is a validated measure for functional capacity in the cancer patient population. Secondary outcome measures included the Short Physical Performance Battery (SPPB) to further assess lower body functionality (balance, gait & sit-to-stand). Improvement in dynamic upper (bicep curl) and lower body strength was assessed using Theraband™ resistance bands. Isometric strength was assessed by handgrip dynamometry. In addition to traditional functional tests, body composition was assessed using DXA, and accelerometers were used to assess energy expenditure and step-count before and after exercise intervention. Lastly, the Edmonton Symptom Assessment System (ESAS) questionnaire to assess HRQOL, and the abridged Patient-Generated Subjective Global Assessment (aPG-SGA) to also assess nutritional components. The secondary aim of the study is to assess feasibility of a 4-week, unsupervised, exercise program in stage 3 and 4 cancer patients without cachexia. Feasibility was evaluated based on: i) recruitment rate, ii) retention rates, iii) test performance, iv) exercise program tolerability and v) adherence. We hypothesized that patients would see improvements in functional scores, overall body strength, and energy expenditure when comparing pre-intervention assessments to post-intervention assessments.

Methods

This study was approved by the McGill University Health Centre Research Ethics Board (MUHC-REB), and they were responsible for monitoring this study. Recruiment and data collection took place through the Cancer Rehabilitation Program of the McGill University Health Centre (MUHC).

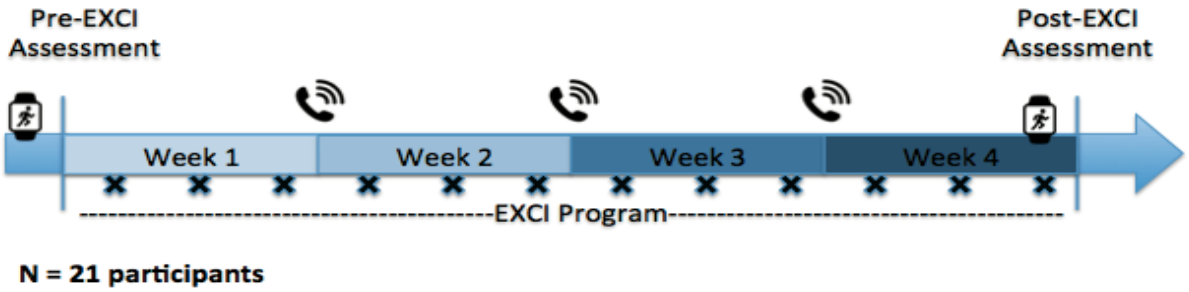
Recruitment took place on clinic days (every Wednesday and Friday) between March 2018 to January 2019. Flyers describing the nature and inclusion criteria of the study were distributed to

eligible candidates and posted in clinic. All patients who fulfilled the following criteria were invited to participate in the study: Patients with stage 3 or 4 cancers who are receiving CRT or other comparable anti-cancer treatments and who are not cachectic according to the criteria defined in Appendix C (Vigano et al., 2016). The study also required that patients be able to ambulate without wheelchair or motorized chair. Patients expecting to receive surgery within the next 6 weeks or, expecting to finish their anti-cancer treatments in the next 4 weeks, were excluded. Contraindications for starting exercise defined by ACSM such as, experiencing fever, extreme fatigue, significant anemia or ataxia were not eligible. All recruited patients received clearance to engage in exercise by a physician and signed the MUHC-REB approved consent form prior to participating in the study. Participants of the study were allowed access to free parking.

Study Design

All study participants (N=21) received consultation with a kinesiologist and were prescribed exercise intervention for 4 weeks in addition to their standard care. The pre-post study design included 21 participants who were assigned the exercise program for 4 weeks (See Figure 1). As seen in Figure 1, participants were assessed before and after the 4-week exercise program intervention. Each participant provided weekly progress reports via telephone to the kinesiologist.

Figure 1: Pre-Post Study Design



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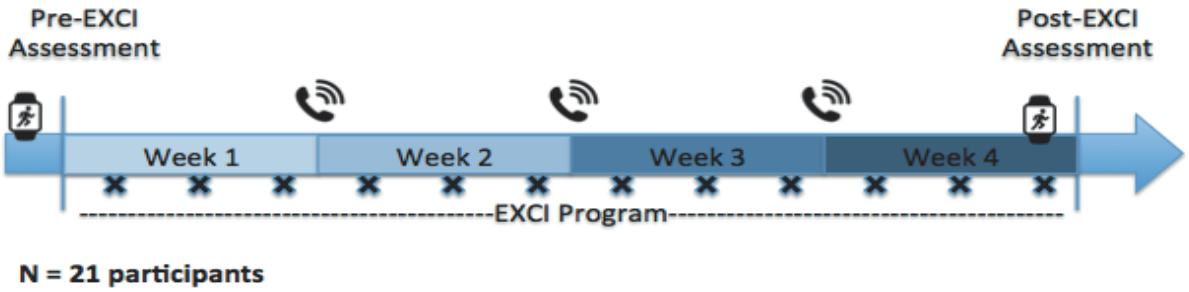


A certified kinesiologist administered each assessment, which lasted no more than 1.5 hours for each visit. All assessments took place at the MNUPAL cancer clinic. Measures for each assessment visit included weigh-ins, functional tests, a handgrip strength test and a DXA scan for tracking changes in body composition. As indicated in Figure 1, participants were contacted through telephone weekly, to discuss their exercise program progress and/or concerns. This way, if the exercise program was becoming too difficult or too easy, the kinesiologist would recommend program modifications or progressions. Moreover, another icon in Figure 1, demonstrates times during which participants were asked to wear an armband to track their activity. Participants were asked to wear SenseWear Pro® activity monitors for 3 consecutive days prior to the intervention, and 3 days prior to the end of the intervention. The activity monitors were useful to track changes in daily energy expenditures in calories and METS, as well as step-count. The 3-day wear time meant that participants wore the armbands when they woke up in the morning and removed it before bedtime, every day, for 3 days. Participants were also asked to complete aPG-SGA and ESAS questionnaires during both assessments in order to assess HRQOL and symptom profiles. An expectation questionnaire was also administered in post-intervention assessment and an exit survey was administered during the final assessment.

Exercise Intervention

As mentioned previously, patients were seen by a trained kinesiologist and prescribed an unsupervised, 4-week long, at home exercise program. During the first patient visit, after baseline assessment was completed, the kinesiologist took the time to thoroughly explain and demonstrate each component and exercise included in the exercise program. Participants were asked to repeat the demonstration to ensure they understood correct form. The exercise program itself included aerobic, resistance, balance and flexibility components. An instruction manual of the exercise program was handed to each participant. The manual included detailed written instruction for each exercise and included images of start point and end point in correct form. We asked that participants to perform the given program at least 3 times per week, totalling 12 sessions over the 4-weeks. Participants were informed that each session should last approximately 40-45 minutes and that activity may be continuous or non-continuous. In other words, the patient could split up components of the program throughout the day to avoid fatiguing quickly. The aerobic portion consisted of a minimum of 15-minutes of self-paced

walking per session, and participants were encouraged to do more if they felt capable. The resistance exercises mainly included seated, closed-kinetic chain exercises for upper and lower body using Therabands™. Resistance training using Therabands™ has been effective in similar home-based exercise programs for older adults and is recognized as a safe method to improve strength and functional ability in older adults and clinical populations (Zion et al., 2003). A total of 5 strengthening exercises for major muscle groups were prescribed, and participants were told to begin with 2 to 3 sets of 6 repetitions per exercise. The following 5 exercises were included: sit-to-stand, seated chest press, seated row, calf raises and seated bicep curls. Most resistance exercises could be done in the seated position using resistance bands (Therabands™) and the kinesiologist demonstrated proper form, always enforcing exhale on exertion, and, most importantly, a neutral spine position, for each exercise. Resistance exercises were expected to take participants ~15 minutes to complete, with short breaks between each exercise. The resistance bands were chosen according to the patient's capabilities shown during their 1st assessment. Participants were advised to begin the program with either a yellow, red or green Therabands™ and were provided with at least 2 extra bands for modification or progression purposes. To determine starting resistance, participants were asked to complete 1 set of 6 repetitions starting with the lightest resistance. At the end of the set, participants were asked if they felt any difficulty completing the set. If so, we recommended beginning with the lightest resistance; otherwise, after a 5 minute rest period, we asked the participant to repeat the set using the next resistance (and so on) until participant felt the resistance provided moderate exertion. This test was repeated each of the 3 exercises requiring the use of a Therabands™. For the balance component, the program included 3 balance positions and we asked that patients practice holding for 15 seconds on each side. These included the feet positioned together; one foot half way in front of the other (semi tandem); and the heel to toe stance (tandem). A list of 4 stretches was also prescribed for the flexibility component (quadricep, chest/bicep, hamstring and back stretch) and participants were to perform them after their walk as a cool-down component. For patients with bone metastasis or spinal lesions, extra precaution called for minor changes in the program to ensure safety (e.g. removing back and hamstring stretches for patients with substantial spinal lesions). To ensure safety, participants were warned to immediately stop exercises if they experienced any alarming pain and to contact the study kinesiologist or physician.

In addition to the program instruction manual, participants were also given a logbook, where they were asked to log details of each exercise performed throughout the 4 weeks. Participants' adherence to the exercise program was rated based on the work recorded in their logbooks (score/ of 12 complete sessions). See Appendix F for an example of pages included in the logbook.

Measures

Outcome measures were selected based on reliability and validity of tests in cancer populations or comparable populations. The following outcome measures were taken during each study visit.

Primary outcome

The 6-minute walk test (6MWT) is used to measure functional walking capacity. The 6MWT evaluates the ability of an individual to maintain a moderate level of PA over a time period reflective of the activities of daily living (Gillis et al., 2014). Subjects were asked to walk back and forth along a 15-meter stretch delimited by an orange cone at each end. Before the start of the test, the assessor instructed participants to cover the greatest distance possible during the test. Patients were allowed to rest during the test if needed, but this rest time is included in the 6 minutes. Each minute, the assessor gave out a standardized motivational message to the participant, as per the American Thoracic Society guidelines. Post administration of the 6MWT, the Borg Rating of Perceived Exertion was used for patients to identify the intensity level of the activity. The total distance covered was recorded by multiplying the total number of laps by 15 meters, then adding the distance covered in the final lap. The 6-minute walk test is valid and reliable in cancer patients, and thus is recommended for use in this patient population (Schmidt et al., 2013). A change in 6-minute walk test distance that falls within a range of at least 19 to 20 m was considered the minimal clinically meaningful difference (Antonescu et al., 2014; Bousquet-Dion et al., 2018; Minnella et al., 2017). To avoid inter-rater variability, the same assessor (FP) took charge of pre and post functional tests.

Secondary outcomes

To further assess lower body functionality, we used the 3 tests that comprise the Short Physical Performance Battery (SPPB). The SPPB was developed to test functionality in seniors; a population in which chronic disease is more prominent and functionality is sometimes compromised (Fisher et al., 2009). This battery is often used in hospitalized older adults, rehabilitation settings, and has been used to assess cancer patients (Fisher et al., 2009). It is often referred to as a 'frailty index' and is an important predictor of all-cause mortality in cancer patients (Pavasini et al., 2016; Guralnik et al., 1994). The SPPB evaluates balance, gait, lower body strength, and endurance by examining ability to stand with the feet together in the side-by-side, semi-tandem, and tandem positions, time to walk 4 meters, and time to rise from a chair return to the seated position 5 times (Guralnik et al., 1994). Each of the 3 tests is timed and scored out of 4 points for a total of 12 points for optimal function.

Handgrip strength was measured using the Jamar hydraulic hand dynamometer (Sammons Preston, Bolingbrook, IL). This test measures the maximum isometric strength of the hand and forearm muscles and is an indicator of general muscle strength (Hamilton et al., 1992). Each participant's grip strength was measured twice on both hands and rounded to the nearest kilogram. The handle was adjusted to the hand by ensuring the proximal interphalangeal joint of the middle finger was at 90 degrees. For handgrip strength assessment, subjects were seated, feet flat on the ground, both knees and test arm bent at a 90-degree angle. The assessor lightly held the base and the readout dial of the dynamometer, and asked the participant to exhale as they squeeze the handle. During the test, participants were given the instruction to "squeeze as hard as you can, ...harder, ...and relax". The average score and peak score were compared to normative data.

Body composition was measured via dual-energy x-ray absorptiometry (DXA; Lunar Prodigy Advance^{TM}, GE Healthcare, Madison, WI). The DXA scan is a reference standard for assessing body composition (Buckinx et al., 2018) and a publication by researchers of MNUPAL has previously validated the use of DXA in advanced cancer patients (Trutschnigg et al., 2008). The GE Healthcare Lunar Prodigy machine was calibrated each day before any patient measurement. Participants were asked to remove any metals and sit with both legs centered on the midline of the scanning bed. Once they laid down supine, their hands were placed in a neutral position with fingers together, thumbs up, and if possible, not touching the thighs. Feet were placed around a

rolled up towel, and held in place with a Velcro strap. For female participants, a Velcro strap was placed around the chest for extra support. The approximate time for the total body scan is 10 minutes. The test printout indicates the amount in kilogram of lean body mass, fat mass, arm lean mass, leg lean mass and the percentage of body fat. Though all these values were recorded, appendicular skeletal mass is likely the most meaningful value for observing changes in muscle mass for the purposes of this study. This is because appendicular skeletal muscle index (ASMI) represents the main portion of muscles involved in PA and ambulation. To calculate ASMI, total arm and leg lean mass were added together and divided by the subject's height in meters squared to obtain the appendicular skeletal muscle index.

Feasibility measures included: patient recruitment, retention, and adherence to the protocol. Participants' adherence to the exercise program was rated based on the work recorded in their logbooks (score/ of 12 complete sessions).

The Edmonton Symptom Assessment System (ESAS) is a validated questionnaire (Bruer et al., 1991) used at the MUHC to assist in the assessment of pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being, and shortness of breath. Each symptom is rated from 0 to 10 on a numerical scale based on severity, with 0 indicating that the symptom is absent and 10 that it is the worst possible severity. The total possible score is 100 and the higher the score, the worse overall HRQOL.

Physical activity/metabolic expenditure during activity was monitored using SenseWear® Pro III Armband Monitors (BodyMedia Inc., Pittsburgh, PA). These activity monitors have been previously validated to measure daily energy expenditure in older adults (Mackay et al., 2011). These multisensor armbands incorporate a biaxial accelerometer that records steps per day, and physiological indicators of energy expenditure. These activity monitors have been used and validated in clinical populations, due to their valid and reproducible estimate of energy expenditure during walking at a slow to moderate pace (Patel et al., 2007), and a high correlation between steps per day and movement counts (Watz et al., 2008; Malavolti et al., 2007). Participants were asked to wear armbands for 3 consecutive days prior to each assessment.

Nutritional status was assessed to help determine presence and degree of cachexia (Vigano et al. 2016). The Abridged Patient-Generated Subjective Global Assessment (aPG-SGA) is a validated questionnaire used to assess the nutritional and functional status of cancer patients. The scoring system allows patients at risk for malnutrition to be identified and triaged for nutritional

intervention. The aPG-SGA may also be useful in monitoring short-term changes in nutritional status. A score ≥9 indicates a critical need for nutritional intervention (Ottery, 2004).

Patient expectation questionnaire: a patient-subjective survey that was developed by the kinesiologist and used to assess exercise program expectations and personal goals before the intervention. See Appendix G.

Patient satisfaction questionnaire: a patient-subjective survey that was developed by the kinesiologist and used to assess tolerance, adhesion, functional perception, enjoyment and overall satisfaction with the exercise intervention. See Appendix H.

Statistical analysis

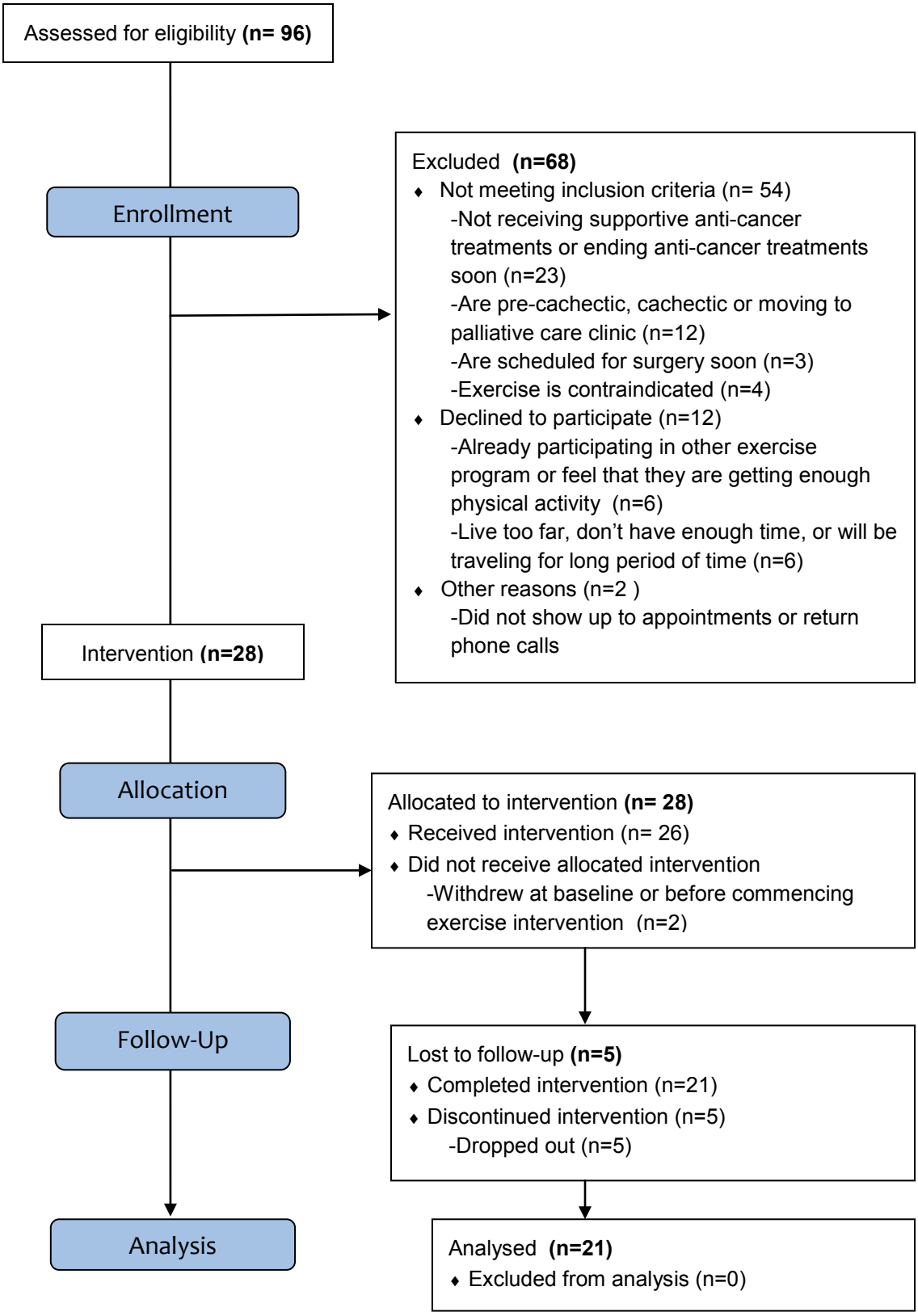
Outcome measures in this study called for quantitative analysis. Our null hypothesis posited that the mean 6-minute walk test performance in the pre-intervention assessment would be the same as that of the post intervention assessment. Analysis included data collected from all 21 patients with exception of one missing body composition scan. Generally, in larger studies, power is set to 0.8, meaning that the study has an 80% chance of ending up with a p-value of less than 5% in a statistical test with a difference that is unlikely due to chance. The calculated sample size required per group, for an α (two-sided) set to 0.05 and power set to 0.8, would have had to be in the proximity of 100 participants according to a Table by Hulley et al. 2013. As such, our small sample size is only suitable for evaluating feasibility or as preliminary data to a future, larger trial with greater sample size and sufficient power. Analyses were performed using NCSS Statistical Software, version 11 (329 North 1000 East, Kaysville, UT). Pre-post intervention results were evaluated using paired t-tests, which compared group means.

Results

Subjects

All details are presented in the CONSORT diagram in Figure 2. According to numbers presented in CONSORT diagram below, retention rate is equivalent to 75% (21/28 = 0.75), calculated drop out rate is equivalent to 25% (7/28=0.25), and recruitment rate is equivalent to 29.16% (28/96=0.2916).

Figure 2: CONSORT diagram



Demographic and Clinical Characteristics

Participant demographic and clinical characteristics were also collected at baseline. Results are summarized in **Table 1**. Calculated mean age was 59 years (SD±14.35) with the youngest participant aged 25 years and the eldest aged 86 years. Women held a small majority, representing 60% of the intervention group. Though the study included a wide range of primary cancer sites, 3 major cancers including, colorectal, lung, and breast represented more than half the group (n=12 of N=21). Most patients (n=13) had stage 4 cancer and a great majority of participants (n=17) were receiving ongoing chemotherapy treatments throughout their study involvement. However, it may be meaningful to note that all patients received chemotherapy as a treatment at some point, whether it was before or during their study involvement. During the study, 4 of the 17 patients on chemotherapy were combining treatments with hormone or immunotherapy. Equally noteworthy, is that 15 of the 21 participants had previously received surgery, and that 6 patients had previously received radiation therapies, though none were ongoing radiation treatment during the intervention. All patients were required to ambulate independently to be eligible for the study, but assistive devices were permitted and 2 patients using canes took part in the study. Remarkably, one amputee also completed the exercise intervention. Cases that demanded extra caution and carefulness in exercise progression included bone metastasis (n=3), CNS lesions (n=3), and axillary cording (n=1).

Table 1: Patient (n=21) Demographics and Clinical Characteristics

Age (years)	59.29 ±14.35
Sex: n (%)	
Female	13 (61.9)[1]
Male	8 (38.01)
Ethnicity: n (%)	
White	19 (90.47)
Non-white	2 (9.52)
Language: n (%)	
French	7 (33.33)
English	14 (66.67)
Primary cancer site: n (%)	
Colorectal	4 (19.05)
Pancreatic	1 (4.76)
Prostate	1 (4.76)
Lung	4 (19.05)
Myosarcoma	1 (4.76)
Ovary	2 (9.52)
Brain	1 (4.76)
Breast	4 (19.05)
Gastric	1 (4.76)
Hodgkins lymphoma	1 (4.76)
Unknown primary	1 (4.76)
Stage: n (%)	
III	7 (33.33)
IV	13 (61.9)
Other grading (brain, lymphoma)	2 (9.52)
Past Treatments Received n (%)	
Chemotherapy	14 (66.66)
Radiation	6 (28.57)
Surgery	15 (71.43)
Immunotherapy	2 (9.52)
Hormone Therapy	2 (9.52)
Ongoing Treatments: n (%)	
Chemotherapy	17 (85.71)
Immunotherapy	3 (14.29)
Hormone Therapy	5 (23.81)
Ambulation and use of Assistive Devices: n (%)	
Cane	2 (9.52)
Amputee	1 (4.76)
Exercise Precautions: n (%)	
Lesions in CNS	3 (14.29)
Bone metastasis	3 (14.29)

Axillary Web Syndrome (Cording)	1 (4.76)
[2]Subjective Fitness Score ($\bar{x}$ ± SD)	
Active rating	4.81 ± 1.86
Decondition rating	6.05 ± 2.18

[1]Numbers in brackets denote percentages.
[2] Participants were asked to rate their perceived fitness levels from 1 to 10 in written baseline questionnaire. A score of 10 signified most active or most deconditionned score. See full questionnaire in Appendix G.

Anthropometrics and Body Composition

Anthropometrics and body composition data were recorded pre and post exercise program and paired t-tests yielded results summarized in **Table 2** (see below). Due to one incomplete DXA scan in post-intervention group, analysis compared pre-inervention group of N=21 to post-intervention group of N=20 for all body composition analyses. Statistical significance was set at $p \leq 0.05$. Average baseline height and weight were 70.93 kg (±18.91) and 1.67 m (±0.09) respectively. Post-intervention weight was slightly increased ($p = 0.063$). Fat mass and body fat percentage were generally maintained. Bone mineral density, lean leg and arm mass, appendicular skeletal mass index (ASMI) were generally maintained and showed no meaningful change over the 4-week program. At baseline, a total of 11 participants were classified as sarcopenic based on ASMI cuttofs defined by Baumgartner et al. (1998). One participant who was sarcopenic before exercise intervention was no longer sarcopenic in post-intervention assessment.

Table 2: Anthropometrics and changes in body composition after the 4-week intervention

	Pre-Intervention (N=21) Mean (SD)	**Post-Intervention (N=21)** Mean (SD)	**P-value**[1]
Weight (kg)	70.93 (±18.91)	71.36 (±18.73)	0.063*
Height (m)	1.67 (±0.09)	-	-
[2]Body Mass Index (kg/m^2)	25.3 (±6.6)	25.5 (±6.5)	0.074
[2]Body Fat (%)	35 (±10.3)	34.3 (±9.2)	0.957
[2]Fat mass (kg)	24.6 (±12.7)	24.7 (±12.8)	0.617
[2]Lean body mass (kg)	42.2 (±8.9)	43.5 (±8.9)	0.066*
[2]Bone Mineral Content (kg)	2.78 (±0.6)	2.80 (±0.62)	0.660
[2]Lean arm mass (kg)	4.36 (±1.38)	4.34 (±1.28)	0.380
[2]Lean leg mass (kg)	13.1 (±3.4)	13.6 (±3.3)	0.258
[2]ASMI (kg/m^2)	6.206 (±1.32)	6.295 (±1.37)	0.463
[3]Sarcopenia			
Yes	11	10	-
No	10	10	

Numbers in brackets denote standard deviation of means (SD). P-values determined using paired T-test.
[1] Significance set to $p \leq 0.05$.
[2] One incomplete DXA scan required analysis of n=20 for post-intervention group.
[3] Sarcopenia based on ASMI cut-offs <5.45 for women <7.26 for men (Baumgartner et al., 1998).
*Denotes trending result.

Functional Outcome Measures

Most functional measures showed significant differences after the intervention (See **Table 3** below). Handgrip strength (HGS) values improved over time with significant increases in mean score (p=0.003), peak score (p=0.004) and associated percentile rank (p=0.006). Short Physical Performance Battery (SPPB) results show significant improvement in repeated sit-to-stand time (p=0.025) and associated point score (p<0.001), resulting in a significantly improved overall SPPB point score (p<0.001). Balance and 4m-Gait-Speed Test (GST) scores did not show statistically meaningful change over time.

Primary Outcome Measure

As seen in **Table 3**, statistically and clinically significant changes were observed in the 6-minute walk test distance (6MWTD) ($p<0.001$). Mean group change in 6MWT distance was +44.2± 38.0m ($\bar{x} \pm$ SD) between pre and post-intervention scores. Refer to **Table 4** for number and percentage of participants having achieved clinically significant changes in 6MWTD. Ratings of perceived exertion using the Borg scale were determined to be "moderate" and were similar pre and post intervention. Both participants with canes chose to perform their 6MWTs without the use of their assistive device.

Table 3: Functional outcome measures over time

Outcome measures	Pre-Intervention (N=21)	Post-Intervention (N=21)	P-value[1]
Hand Grip Strength (kg)			
Mean score	30.54 (±9.61)	31.61 (±9.57)	0.003*
Peak score	32.76 (±9.54)	34.19 (±9.98)	0.004*
Peak Percentile	55.79 (±29.60)	61.61 (±29.87)	0.006*
Short Physical Performance Battery (time)			
4-Meter Gait Speed	3.77 (±0.84)	3.59 (±0.78)	0.467
Repeated sit to stand	15.67 (±5.06)	12.69 (±3.0)	0.025*
[2]Short Physical Performance Battery (points)			
Balance	3.76 (±0.54)	3.76 (±0.54)	1
4-Meter Gait Speed	3.85 (±0.36)	3.90 (±0.3)	0.643
Repeated sit to stand	2.19 (±1.08)	3 (±1.05)	<0.001*
Total (*x*/12)	9.81 (±1.36)	10.66 (±1.39)	<0.001*
6-Minute Walk Test (m)	413.1 (±92.2)	457.3 (±106.2)	<0.001**
[3]Borg Scale Score	11.285 (±2.37)	11.523 (±2.54)	0.682

Numbers in brackets denote standard deviation of means (SD). P-values determined using paired T-test.
[1] Significance set to $p \leq 0.05$.
[2] Each of the 3 tests included in this battery, were score in points according to results tables provided in SPPB testing guidelines. Each of the tests were scored on a total of 4 points, for a grand total score over 12 points.
[3] Borg scale was used to measure ratings of perceived exersion after 6MWT.
* Denotes statistically significant result.
** Denotes statistically and clinically significant result.

Table 4: Number of participants achieving clinically significant change in 6MWT distance

Clinically significant change in 6MWT distance	
[1]Group mean difference in 6MWTD ($\bar{x} \pm$ SD)	+44.2± 38.0m
Number and percentage of participants achieving:	
[2]MCMD (>20 m difference in 6MWTD)	17 (81%)
Improvement ≤20 m difference in 6MWTD	3 (14%)
Deterioration in 6MWTD	1 (5%)

[1]6MWTD = 6-Minute Walk Test Distance
[2]MCMD =Minimal Clinically Meaningful Difference for 6MWT as defined by Antonescu et al. 2014; Bousquet-Dion et al., 2018; Minnella et al., 2017.

Activity Monitor Data

Energy expenditures were also recorded 3 days prior to the start and before the end of the intervention. Results generated by the SenseWear Pro® activity monitors include daily stepcount and energy expenditures in both calories and metabolic equivalents (METs). Activity monitor data is summarized in Table 5 below. The monitors are programmed to identify sedentary, moderate and vigourous activity based on programmed MET cut-offs. For the purpose of this study, any energy expenditure (EE) <3 METS was considered sedentary behaviour; EE ≥3 METs and ≤ 6 METs was considered "moderate" PA; and EE >6 METs and < 9 METs was considered vigorous PA. As seen in **Table 5**, most activity monitor results were highly significant and reflect increased average stepcount ($p < 0.001$) and EE ($p < 0.001$) post-intervention. Notably, most increases in EE are due to increases in moderate PA rather than vigorous PA, but both moderate and vigorous activities show significant increases after the exercise program ($p < 0.001$ and $p = 0.039$ respectively). Lastly, sedentary behaviour showed an overall decrease though it was not enough change to be statistically meaningful.

Table 5: Activity Monitor Data over Time

Outcome measures	Pre-Intervention (N=21)	End-Intervention (N=21)	P-value[1]
[2]Daily Average EE			
Kilocalories	1775 (±412)	2142 (±470)	<0.001*
METs	1.53 (±0.3)	1.72 (±0.31)	<0.001*
Number of Steps			
Daily Average	3576 (±1565)	4943 (±2052)	<0.001*
Peak (best day)	4715 (±2651)	5973 (±2606)	<0.001*
[3]Daily Average "Active" EE (kcal)	291.47 (±306.65)	461.98 (±367.1)	<0.001*
[4]Daily Average PA Duration (hrs)			
Total	1.03 (±0.96)	1.70 (±1.25)	<0.001*
Moderate	1.018 (±0.96)	1.64 (±1.17)	<0.001*
Vigorous	0.009 (±0.024)	0.05 (±0.1)	0.039*
Daily Average Sedentary Behaviour Duration (hrs)	11.20 (±2.55)	10.59 (±2.35)	0.166

Numbers in brackets denote standard deviation of means (SD). P-values determined using paired t-test.
[1] Significance set to $p \leq 0.05$.
[2] EE=Energy Expenditure; METs= Metabolic Equivalent or kcal/kg/hr; PA=Physical Activity; kcal = kilocalories; hrs = hours
[3] For the purpose of this study, PA or "Active" Energy Expenditure represents an EE ≥3METs.
[4] For the purpose of this study "moderate" PA represents an EE ≥3 METs and ≤ 6 METs; "vigorous" PA represents an EE >6 METs and <9 METs.
* Denotes statistically significant result.

Symptom and HRQOL assessment questionnaires

Abridged PG-SGA and ESAS questionnaires were used to assess symptoms and HRQOL before and after the intervention. Total scores for each questionnaire were analyzed but did not bear statistically significant results (See Appendices D and E to view full questionnaires). Note that, from the symptoms rated in the ESAS questionnaire, pain was generally rated lower post-intervention and demonstrated a statistical trend ($p = 0.06$). Questionnaire total score results, as well as results from each subsection, are summarized in **Table 6** below.

Table 6: Pre-Post Intervention Subjective Symptom Assessment Questionnaires

Outcome measures	Pre-Intervention (N=21)	Post-Intervention (N=21)	P-value[1]
[2]aPG-SGA			
Total Score	4.71 (±2.81)	4.47 (±3.50)	0.751
Section 1	0.76 (±1.18)	0.9 (±1.14)	0.613
Section 2	0.24 (±0.44)	0.29 (±0.72)	0.789
Section 3	2.86 (±2.83)	2.38 (±2.58)	0.487
Section 4	0.86 (±0.73)	0.90 (±0.70)	0.665
[3]ESAS			
Total Score	27.66 (±19.27)	23.04 (±16.76)	0.143
Pain	3 (±2.70)	2.3 (±2.98)	0.06*
Tiredness	4.3 (±2.24)	4.05 (±2.62)	0.548
Nausea	2 (±2.66)	1.9 (±2.59)	0.837
Depression	2.9 (±3.14)	2.05 (±3.27)	0.189
Anxiety	2.52 (±2.86)	2.14 (±2.22)	0.596
Drowsiness	3.67 (±3.08)	3 (±3.07)	0.134
Appetite	2.38 (±3.02)	1.9 (±2.66)	0.45
Well-Being	3.81 (±2.29)	3.24 (±2.60)	0.168
SOB	2.33 (±3.14)	2.33 (±2.69)	1

Numbers in brackets denote standard deviation of means (SD). P-values determined using paired T-test. aPG-SGA = Abridged-Scored Patient-Generated Subjective Global Assessment (See Appendix E) ; ESAS = Edmonton Symptom Assessment System (See Appendix D). Lower scores denote better health related quality of life in both questionnaires. SOB=Shortness of breath

[1] Significance set to $p \leq 0.05$.

[2] Refer to Appendix E to view each aPG-SGA questionnaire section and how each is scored.

[3] Refer to Appendix D to view ESAS questionnaire symptom list and how each is scored.

*Trending result.

Exit Survey Scores, Logbook Adherence

After the exercise intervention was completed, an exit survey (see Appendix H) was used to assess patient satisfaction with the exercise program. The exit survey required patients to score tolerance, motivation, function and enjoyment of the exercise program on a scale of 1 (lowest) to 5 (highest). An average score out of 5 was calculated for each factor and results are presented in the first 4 rows of **Table 7**. Reasons for missing training sessions were also quantified and the most frequent answer proved to be fatigue with 13 participants (~62%) reporting this reason for missed sessions. Pain and other symptoms were also listed as reasons for missing exercise sessions by nearly 40% of participants.

The exercise data obtained from patient logbooks were also analyzed in order to assess adherence to the exercise prescription. Because the exercise program called for a total of 12 sessions (3 sessions/week for 4 weeks), completion of each component of the program (cardio, resistance, balance and flexibility) was tallied out of 12, in order to obtain a total score out of 48 for overall adherence. On average, the patients completed approximately 85% of the exercise sessions.

Table 7: Post-Intervention Exit Survey Scores and Logbook Adherence

Outcome measures	
Tolerance (*x*/5)	4.09 ±0.94[1]
Motivation (*x*/5)	3.74 ±0.92[1]
Improved Function (*x*/5)	3.64 ±0.94[1]
Enjoyment (*x*/5)	4.40 ±0.66[1]
Possible Reasons for Missing Training Sessions: n (%)	
Fatigue	13 (61.9)
Pain or other symptoms	8 (38)
Lack of time	3 (14.3)
Too difficult	0
Other	6 (28.5)
Adherence: n (%)	
Cardio (*x*/12)	11.1 ±1.61 (92.5)
Resistance (*x*/12)	10.14 ±1.96 (84.5)
Balance (*x*/12)	9.19 ±3.63 (76.6)
Flexibility (*x*/12)	10.24 ±3.03 (85.3)
Total Adherence Score (*x*/48)	40.67 ±6.8 (84.7)

Numbers in brackets denote percentages.
[1] Participants were asked to rate their perceived tolerance, motivation, functional change and program enjoyment in a post intervention exit survey. Scales were from 1 to 5 (best outcome). See full questionnaire in Appendix H.

Theraband Use and Progression

Lastly, we quantified the use of each Therabands™ based on the frequency each band color appeared in participant logbook records for each exercise. Out of the 5 resistance exercises prescribed, 3 exercises required the use of Therabands™ (seated chest press, row and bicep curl). The remaining 2 exercises were excluded from this analysis because they generally used body

weight rather than Therabands™ (Sit-to-Stand & calf raises). Different colors represent a different resistance and are listed from the least to the most resistance in **Figures 3, 4 and 5** (yellow, red, green, and blue). In terms of most commonly used resistance bands, the majority of participants reported using the red band (90.5%, n=19) at least once, at some point throughout the program. The second most frequently used color was the green band, and was used by 76% (n=16) of participants, at least once, at some point during the study. Because each color-band corresponds to a resistance in kilograms at 100% elongation, we were able to quantify the group's total resistance for every exercise, every week, and view their overall progression. To view color bands' associated resistance in kilograms at 100% elongation see Appendix I or refer to legend of **Figures 3, 4 and 5**. Represented in **Figures 3, 4 and 5** below, you will see the number of participants that reported using each color band, every week. In addition, under each week is the total calculated resistance for the group (in kg) and the corresponding collective percent increase in resistance from the previous week. Lastly, the overall percent progression is bolded under each figure and ranged between 21-29% increase between weeks 1 and 4. Paired t-tests between resistances used in week 1 and week 4, show that strength progression for the chest press (1.64 ±0.29 vs. 1.98 ±0.32 kgs; $p<0.001$), seated row (1.66 ±0.24 vs. 2.06 ±0.32 kgs; $p<0.001$), and bicep curl (1.55 ±0.23 vs. 2.0 ±0.28 kgs; $p<0.001$) was significantly increased over time.

Figure 3

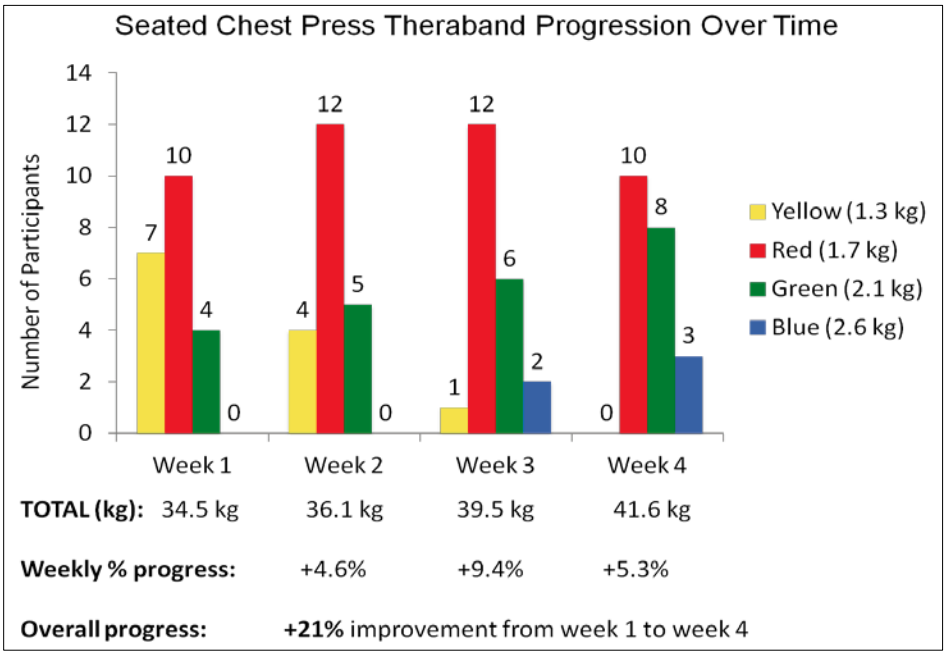


Figure 4

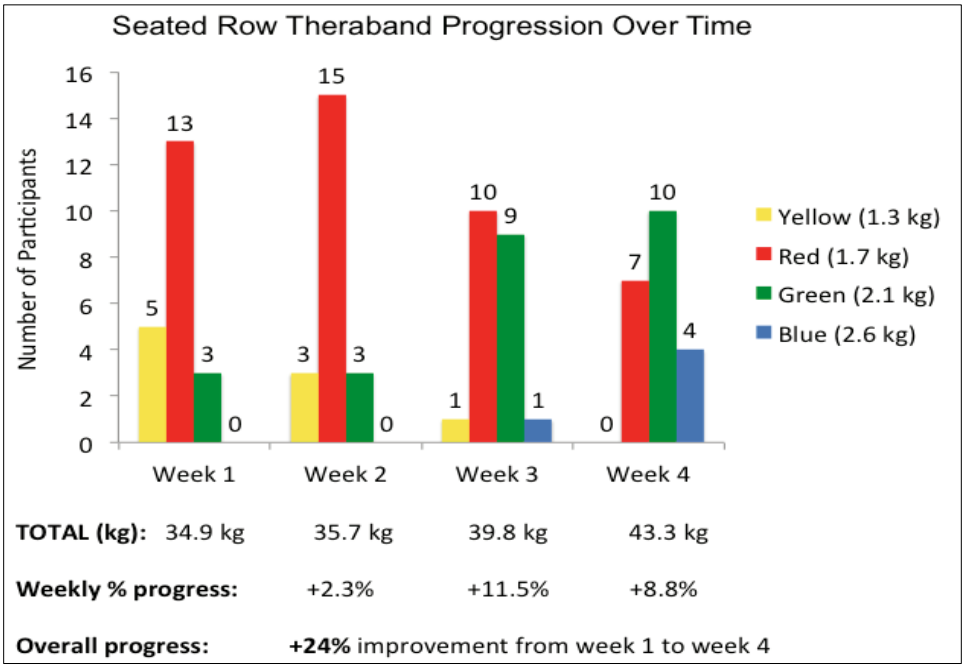
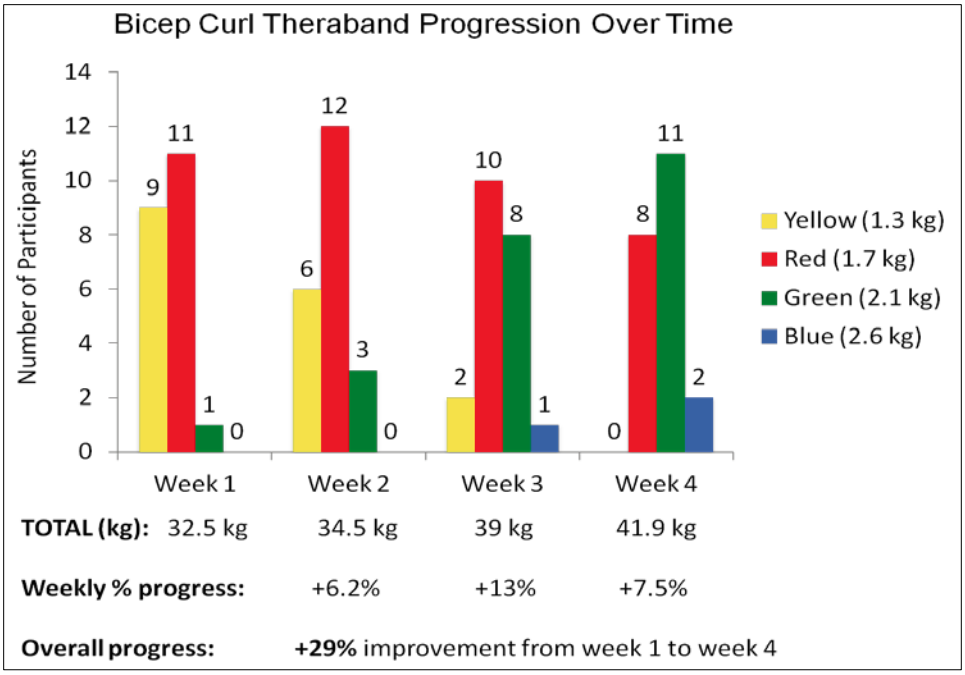


Figure 5



Discussion

Recruitment rate, Dropout rates & Adherence

Based on figures from the CONSORT diagram (**Figure 2**), we reported a dropout rate of 25% and a recruitment rate of 29%. These figures are comparable to findings by Oldervoll et al. (2004), who reviewed results of 12 similar exercise interventions in cancer populations. This review reported varying drop-out rates up to 34% and average recruitment rate of 43% (Oldervoll et al., 2004). Though our study reports a smaller recruitment rate, this is likely owed to more specific inclusion criteria in order to screen for cachexia. In addition, our study focused on more advanced cases than those reviewed by Oldervoll (2004), many of which were non-curative, and thus, more difficult to recruit. For these reasons, we do not expect to generalize this study's findings to all cancer patients, but to better understand the impact of the current exercise prescription in a more specific group (advanced supportive care cancer patients without cachexia). Oldervoll et al. (2004) also reports an average adherence rate to exercise prescription of 72%, for which, our study reports 85% based on participant logbooks (See **Table 7**). One possible reason for the study's successful adherence rate may be due to our weekly phone check-ins which encouraged adherence to the exercise program. A high adherence rate may also be attributed to our study's relatively short (4 week) intervention period, as compared to studies reviewed by Oldervoll et al (2004), which were generally longer than 6 weeks. Based on our results, a four week exercise program is sufficiently long to demonstrate significant changes in 6MWT, strength, and energy expenditure and is more amenable to retaining advanced cancer patients than longer interventions.

Demographics and Clinical Characteristics

In terms of subject demographics, we included different ages, and mixed cancer diagnoses, which allowed for better recruitment rate. Leading cancers were well represented in our sample given that 3 major cancers including, colorectal (n=4), lung (n=4), and breast (n=4) represented more than half the group (n=12). Over 80% of participants were receiving chemotherapy during their study involvement, but all participants received chemotherapy at some point in their cancer journey. The few patients who were not receiving chemotherapy during the study intervention remained on hormonal or immune therapies. Furthermore, over 70% of participants received cancer related surgeries prior to study involvement. In sum, all

participants received treatments which, they felt, contributed to the demise of their normal functioning. As indicated in **Table 1**, most patients reported low self-perceived Fitness Scores in baseline questionnaire, rating their "level of de-conditioning" ($\overline{x}$ ± SD; 6.05 ± 2.18) higher than their "level of activity" ($\overline{x}$ ± SD; 4.81 ± 1.86) on scales of 1 (lowest) to 10 (highest).

Body composition

Concerning changes in body composition measures, DXA scans revealed little significant change over the 4-week exercise intervention. This is likely due to a relatively short intervention period, not allowing enough time to quantify much physiological change. However, despite little statistically significant change in body composition, one may note that some group means are trending in promising directions, especially in terms of lean mass (p=0.0066), which was generally increased post-intervention ($\overline{x}$ ± SD; 0.74 ± 1.6 kg). Increase in weight was also trending (p=0.063), with no significant change in body fat percentage or fat mass, indicating that weight gain was more possibly due to increases in lean mass. Most importantly, participants were generally able to maintain their body composition over the 4-week exercise program, despite the cumulative fatigue, and effects of treatments, that may have otherwise solicited deterioration (Freedman et al., 2004).

Functional Testing

Though body composition statistics did not indicate much change, functional testing revealed more significant results. Notably, results of the primary outcome measure showed both statistically and clinically significant changes in 6MWTD. Clinically significant change in 6MWTD was attained by those achieving a minimal clinically meaningful difference (MCMD) value >20m as defined and observed by others (Antonescu et al., 2014; Bousquet-Dion et al., 2018; Minnella et al., 2017). Consequently, results indicate that 81% of participants (n=17) showed clinically significant improvement (>20 m) in their walking capacity post-intervention, with but one participant showing regression.

Total functional score provided by SPPB also showed statistically significant improvement post intervention (p<0.001). Given that the sit-to-stand exercise was performed by participants over the 4 weeks, significant change in this test was unsurprising. In fact, it is important to note that change in total SPPB score was mostly attributed to significant changes in

repeated sit-to-stand test performance ($p<0.001$). Both 4-m gait speed test and balance test did not demonstrate meaningful change over time ($p=1$ and $p=0.643$ respectively). Pre-post balance scores did not change at all, as most participants scored 100% of their points in their first visit, reaching a performance ceiling even before commencing exercise intervention. As such, the balance test was not considered sufficiently sensitive to change, and poses an insensitive-measure bias in this population. An alternative, balance test to use in this patient population is the single leg stance test, which is more difficult and sensitive to change.

Although improvements in functional performance are not necessarily reflected by important changes in our reported body composition measures, improved functional performance can be attributed to many other factors. For instance, cardiorespiratory changes, like increased $VO_{2peak,}$ can increase walking capacity and translate to improvements in shuttle walk tests (Singh et al., 1994; Quist et al., 2012). Alternatively, increased motor unit recruitment, can explain early improvements in performance even without muscle hypertrophy (Moritani and deVries, 1979). In turn, an improved symptom profile (e.g. pain symptoms), can motivate participant to perform better (Reis et al., 2018).

Activity Monitor Data

Very few advanced cancer studies to date have reported using accelerometers, even though they are best suited to provide objective measures of energy expenditures (Broderick et al., 2013). Instead, most studies rely on self-report measures (Dahele et al., 2007). Broderick et al. (2013) suggest that, accelerometry may be the best measure of PA in cancer-based studies, because of high accuracy and minimal wearer burden. In current cancer publications, some small studies have reported the use of accelerometers (Freeny et al., 2011; Guinan et al., 2013; Walsh et al., 2010), and there are reports of increased use in recent, larger cancer-survivor studies (Lynch et al., 2007; Courneya et al., 2012). However, none of these studies examine pre-post exercise differences in energy expenditures and step counts for supportive care patients.

In the present study, meaningful changes in energy expenditures imply that prescribed exercises promoted the adoption of more active behaviours. One may note that pre-intervention daily average energy expenditures (EE) and stepcounts were very low according to the American College of Sports Medicine (2014) that stated that energy expenditure under 3 METs is considered “sedentary behaviour” or “light activity”. Likewise, according to Tudor-Locke et al.

(2004), daily step-counts under 5000 steps are categorized as "sedentary or inactive lifestyles". Thus, averages of daily EE of 1.53 METs and step-count of 3576 steps/day reflect a highly inactive and deconditioned group at baseline. In terms of kilocalories spent in PA, only 16% (291 calories/day) of the total 1775 kcals/day were expended actively (>3 METs), based on baseline data. According to Ainsworth et al.'s (2011) compendium of physical activities, for a person weighing ~73kg (160 lbs), 290 kcals could represent an hour of gardening or raking the lawn for example. In comparison, for the post-intervention value of 460 kcals expended in PA, Ainsworth et al.'s (2011) compendium of physical activities, describes activities like an hour of hiking or shovelling snow for a person of equal weight. On average, at the end of the intervention, participants expended 22% (462 calories/day) of their total EE (2142 kcals/day) in PA (>3 METs). In other words, participants expended significantly more calories engaging in activities >3METs after the exercise intervention. In terms of stepcount, the group showed a total average increase of 1367 (±910) steps (~38%) in end-intervention from baseline. Hence, results from accelerometers post-intervention, show a trending increase in EEs, step-count and PA. Regarding time spent in PA (>3METs), results indicate a total increase of 0.62 hrs (or +37 mins) of PA per day when comparing pre vs. end-intervention PA duration. The increase in PA duration is largely attributed to increase in moderate activity, with a very small, but equally significant, increase in vigorous activity. To conclude, though increases in energy expenditure were sufficient to significantly reduce body weight or percent body fat over the 4 weeks, the important fact remains that most participants increased their activity levels considerably from baseline.

Questionnaires

We also compiled results from symptom management questionnaires aPG-SGA and ESAS and found there to be little change between pre-post intervention scores. In fact, total score for aPG-SGA was relatively maintained, implying that participants did not perceive considerable change in their symptom profile or HRQOL in the 4 weeks since baseline. Similarly, total ESAS score did not prove to be statistically significant, despite a more promising drop in overall score. Comparably, other short-term studies also found no remarkable change in HRQOL and symptom profiles (Dimeo et al., 2008; Adamsen et al., 2003). It may, however, be worth noting that, participants rated their perception of pain significantly lower than at baseline.

Therefore, it is possible that the perceived decrease in pain is owed to mechanical or neuromuscular improvement on account of the exercise intervention, similar to reports in other studies (Reis et al., 2018; Do et al., 2015). However, reduction in pain may also be due to other interventions on account of standard care (e.g. new drug prescription), and, thus, the study would necessitate a control group to better examine the direct effects of the exercise intervention. All in all, given that patients continued receiving anti-cancer treatments throughout their study involvement, it is reasonable to expect continuing symptoms and side-effects throughout the study, and it is important to recognize that patients did not feel like their condition deteriorated over the 4-week intervention. This observation is supported by the fact that HRQOL and symptom profiles were generally well maintained.

In regards to results from the exit survey, we may conclude that the prescribed exercises were well tolerated by the majority of participants ($\overline{x}$ ± SD, 4.09 ± 0.94 on a scale from 1 to 5). Additionally, most participants claimed to enjoy their experience with the exercise program ($\overline{x}$ ± SD, 4.4 ± 0.66) and were usually motivated enough to complete the sessions ($\overline{x}$ ± SD, 3.74 ± 0.92). The majority of participants also reported self-perceived improvements in function with an average score of 3.64 ± 1.86 ($\overline{x}$ ± SD) on a scale of 1 to 5, which agrees with improvements seen in our study's functional outcome measures. With regards to possible reasons for missing exercise sessions, the most cited cause was "fatigue" (reported by n=13, 62%), followed by "pain or other symptoms" (reported by n=8, 38%). In other words, patients were more likely to miss an exercise session because of presenting symptoms, and not because the program was too difficult or due to a lack of time. Having said this, participants did not seem to miss too many exercise sessions, given that our total adherence rate was 85%. Upon a closer look at reports in logbooks, balance exercises were the most likely to be neglected (balance adherence = 76.6%), and cardio sessions were most rarely passed up (cardio adherence = 92.5%).

Theraband Progression

To date, very few cancer studies using Therabands™ (Gillis et al., 2014, Gillis et al., 2016, Bui et al., 2019) will detail band progression in their results. Information regarding exercise progression is especially important in clinical populations such as advanced, supportive care cancers, because exercise prescription guidelines are either vague or lacking. We have outlined our cohort's collective progression (in kg and percentage) from week 1 to week 4. Our

results revealed that change in resistance from week 1 to 4 was statistically significant for each of the 3 exercises. There was a clear progression between each week, but the greatest progressions were between weeks 2 and 3. At this point in time, most participants had progressed from the color band they started with in week 1. The bicep curl exercise showed the greatest collective improvement because more participants started with lighter resistances (yellow or red), perhaps, given that it is a smaller muscle group. We also note that the most frequently used bands are red and green for this clinical population. Though similar short-term cancer studies also demonstrate improvements in strength (Adamsen et al, 2003, Quist et al., 2012), they did not measure body composition or changes in lean mass. Once more, despite insignificant change in our participant's lean arm mass, early neuromuscular adaptations, such as improved motor unit recruitment, could be responsible for observed improvements in strength in the absence of hypertrophy (Moritani and deVries, 1979).

Conclusion

Our findings imply that 4-week, unsupervised, resistance and walking training program, is beneficial to, and well tolerated by, advanced cancer patients in supportive care. Comparisons between pre-post intervention outcome measures revealed promising improvements in functional performance, namely, clinical and statistical increase in walking capacity. Further, lower body strength showed significant improvements based on meaningful change in time required to perform 5 sit-to-stand repetitions. Similarly, upper body strength showed improvement based on Theraband™ progression analysis, as well as, significant increase in HGS results. Activity monitor data (collected with SenseWear Pro®) indicates significant increases in EEs at the end of the intervention, with more calories expended in PA than at baseline, even, after only 4-weeks. Although change in EE was not sufficient to significantly alter body composition values in a 4-week time frame, a promising trend in increasing lean mass, combined with improved walking capacity and strength, could indicate the beginnings of more significant change in body composition, and more research is required to observe body composition, and PA patterns, perhaps, over a longer period of time and post-intervention. In addition, HRQOL and symptom profile were well maintained throughout the 4-week exercise programs, with no marked deterioration, despite continuing treatments. In fact, a trending decrease in pain was observed post intervention and requires more controlled research to investigate if we can credit this change

to the exercise intervention. Because of our study's small sample size and limited resources, we must recognize some important limitations, which are highlighted in the following chapter. Fortunately, our study protocol showed optimistic feasibility based on positive recruitment rate, retention rates and adherence, all of which encourage the opportunity for a future randomized control trial. As such, the following chapter will also discuss potential future directions of this work. In sum, our study results encourage the combined use of Therabands™ and self paced-walking as a safe, well-tolerated, and functionally impactful exercise prescription even after 4-weeks time. In clinical terms, we conclude that 4-week prescriptions combining resistance and self-paced walking exercises may be used to increase walking capacity and energy expenditure, as well as, help maintain muscle mass in patients undergoing anti-cancer therapies.

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Chapter III

Conclusion

Concluding remarks

Our study results support many benefits of exercise, despite its short 4-week time frame. Based on this study's findings and similar findings in previous research, safe, light-to-moderate exercise intervention should be encouraged in advanced cancer patients at least 3 times/week. Further, because our study focused on patients who have not been afflicted by cancer cachexia, and, was well received, we can assume that the given prescription was a suitable starting point for this patient population. In regards to future direction, it would be interesting to compare non-cachectic patients to those afflicted by cancer cachexia, in terms of how differently they would respond to the given intervention. However, as mentioned previously, it is also important to recognize the limitations of the current study in order to optimise future research and larger scale randomized control trials (RCT). The following sections, will examine limitations and future direction of this work.

Limitations

Given that, the current study is a pilot study we do not expect to generalize the results of this small cohort. Based on the calculated effect size, a future RCT would require ~100 participants per arm in order to sustain power of 80% ($\alpha = 0.8$) (Hulley et al., 2013). In addition, an RCT would call for a control group where participants are not receiving the prescribed exercise intervention. Because our analysis did not compare findings to a control group, it does not measure the effects of standard care against those of the exercise intervention.

Our current study also helped us identify some technical limitations. In terms of the DXA, potential errors can occur through technical error or biological variation (Lohman et al., 2000; Nana et al., 2015). Technical errors would include variation induced by calibration or failure to calibrate, and variations in positioning or regional analysis of the participant (Toomey et al. 2017). Biological variation could occur by effects of food, fluid intake, and hydration status before measurement (Toomey et al., 2017). For instance, the DXA machine, used to assess body composition, does not recognize edema or fluid retention in patients, and, instead, will identify edematous tissues as lean mass. Because lymphedema is a reality for a number of cancer patients, future studies should consider screening for lymphedema, to avoid possible overestimations in lean mass. Similarly, hydration status is also relevant when assessing body

composition, especially for patients receiving treatment, because significant water retention or dehydration can occur by adverse effect (Behar et al., 2003; Sarhill et al., 2001). In the current study, one participant was asked to return for final weigh-in and DXA scan, because she was visibly swollen after receiving treatment, and, by the next day, her water retention had visibly decreased. In the present study, fluid hydration status was not controlled. Though, it may be difficult to control for this, reducing this bias would involve estimating similar assessment times in relation to specific time points in treatment cycles.

Another limitation of the study that could help explain little change in body composition is that no nutritional component was involved in the intervention. A number of multimodal studies suggest that combining nutrition and exercise can better help preserve muscle mass, but more research is required to support this claim (Gillis et al, 2016; Gillis et al. 2014, Bui, 2019).

In regards to group demographic, our cohort included a variety of different baseline capacities, a wide range of ages, and different cancer types. We also had slightly more women than men participants, but sample size was too small to make sex comparisons, or comparisons between aforementioned demographic variables. Whilst we cannot ignore possibility of a heterogeneity bias, it seems the group was homogeneous enough to show collective improvements in function and active behaviour. In larger sample sizes, demographic and clinical comparisons can be made between groups, to control for variability of outcome measures. Other sources of variability in advanced cancer populations could include patients with bone metastasis, axillary cording, and lymphedema, but more research is needed to examine this front.

Naturally, each outcome measure also has its limitations. In terms of functional assessment tools, we noted that tandem balance tests had a really high success rate at baseline, and left little opportunity to assess improvement post-intervention. As such, we recommend the use of a test with a higher performance ceiling (e.g. single leg stance) in future works. In terms of our primary outcome measure, the 6MWT, we used the same long corridor for each assessment, to limit the number of turns and reduce variability. Because the same assessor (FP) performed pre-post outcome measures, we avoided inter-rater variability, but experimenter's bias is possible. Another possible source of variability in 6MWTD is the learning curve associated to the test. According to Spencer et al. (2018), to eliminate learning curve bias and increase accuracy, we would need to perform a practice shuttle walk before the true test.

In regard to activity monitors, there does not seem to be a clear consensus on the minimum wear time required for valid monitoring (Broderick et al., 2014). Masse et al. (2005) propose that a conservative estimate lies between 3 to 7 full 10 hour days, or days for which 60% of waking hours are represented. According to Pitta et al. (2005) minimum requirements to assess PA in daily life is 2 days. However, a cancer population study conducted by Maddocks et al. (2010), recommends up to 6-days of monitoring to best reflect habitual levels of activity. Our study examined activity monitor data from 3 days' wear before and after exercise intervention, meeting the proposed "minimum" requirements. Participants were instructed to wear armbands when they woke up in the morning until bedtime, which covered at least 60% of waking hours. Lastly, it has been suggested that weekend days and weekdays need to be sampled (Gretebeck et al., 2005) since there's a possibility of EE differences between weekdays and weekend days.

Lastly, given that the intervention was unsupervised, we could not verify logbook records obtained by participants. Some might argue that, because of this, progression may have been limited, given the lack of trainer motivation and security, during training sessions. If resources permit it, supervision of at least one of three training sessions per week could further encourage progression and motivation. To otherwise fulfill a sense of encouragement and security, it was important to include weekly phone check-ins with participants and remain accessible by phone to answer any concerns.

Future Direction

Though our study was limited by several factors, we find that it is sufficiently feasible to replicate, and develop into a larger-scale RCT. In practice, our results show that significant change in 6MTD, strength, and energy expenditures are achievable in a relatively short 4-week period. Given the functional impact and high adherence rate associated to this time frame, 4-week exercise interventions are recommended to similar future works. Moreover, our study results encourage the combined use of Therabands™ and self paced-walking as a safe, well-tolerated, and functionally impactful exercise prescription. Future interest would lie in comparing how pre-cachectic and cachectic groups respond to similar exercise interventions. Adding a nutritional component to future works could also shed light on the impact of combined interventions versus exercise alone in each of these patient populations. As mentioned

previously, a RCT would require ~100 participants in each arm to confirm results are not experimental error. To conclude, much more research is required to optimize the specificity and safety of exercise guidelines in a population as variable as advanced, supportive care, cancers.

Chapter IV

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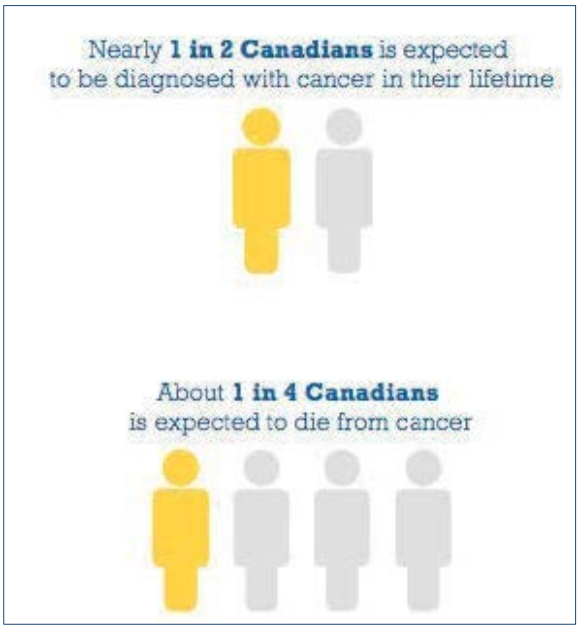
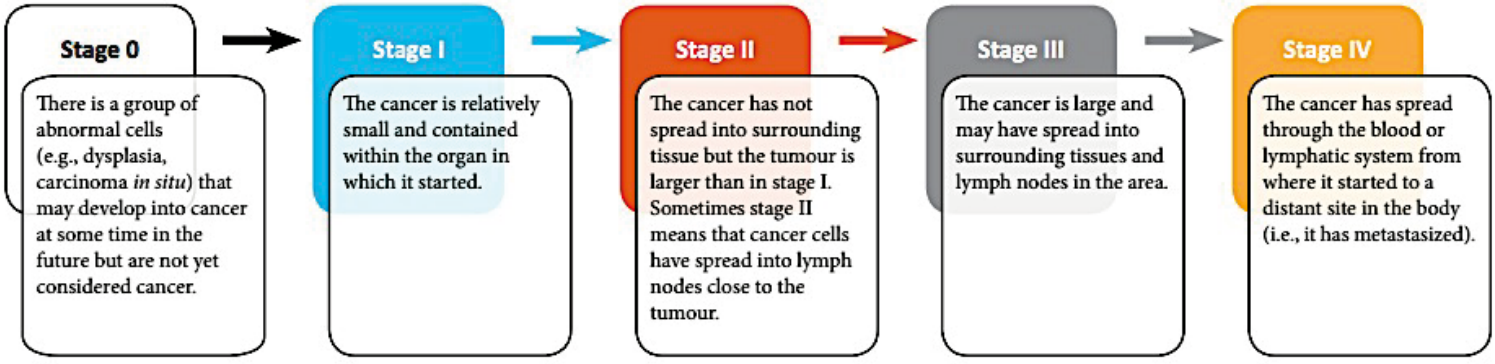
Appendix A – Canadian Cancer Statistics (2018)



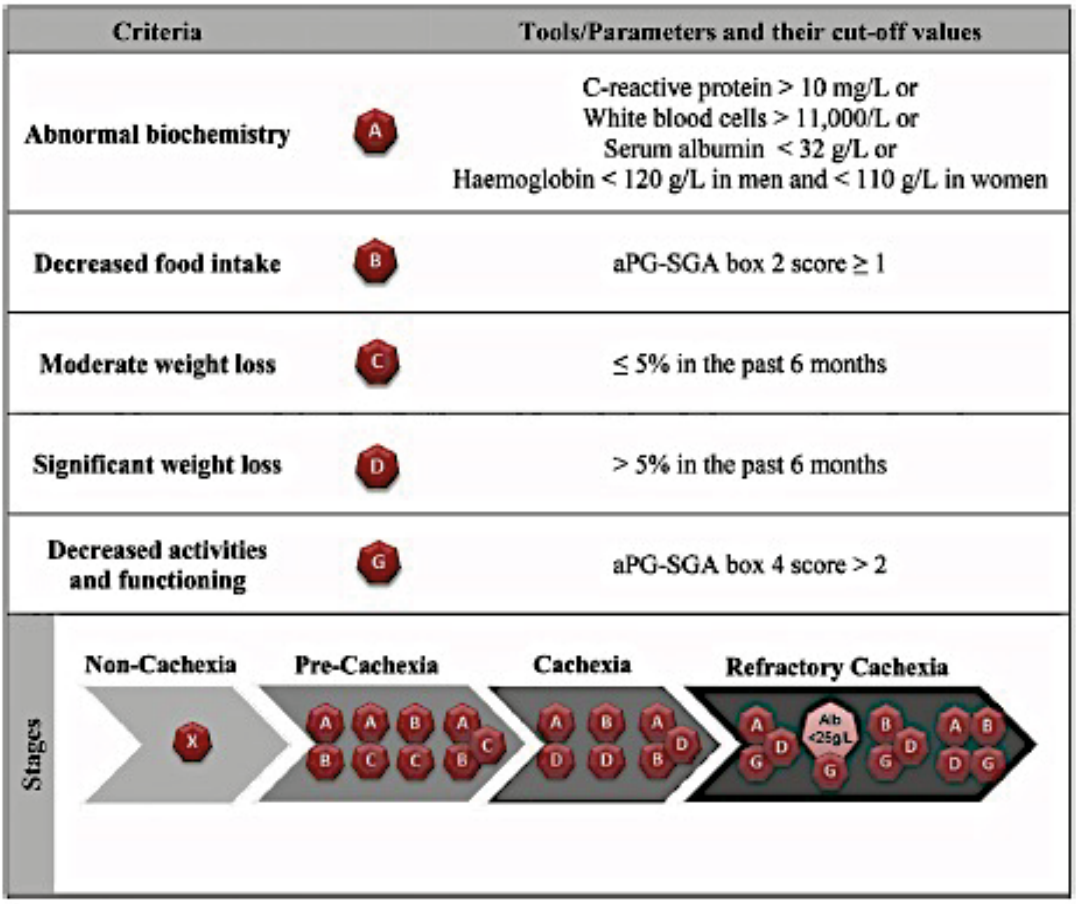
Appendix B – Cancer "TNM" Staging System

Canadian Cancer Society (2018)



Sometimes uppercase letters are added to the number to divide these categories into substages.

Appendix C – Vigano et al. (2016) Cancer Cachexia Classification System



aPG-SGA: abridged Patient-Generated Subjective Global Assessment
(box 2 – food intake; box 4 – activities and functioning); X: insufficient number of criteria or criteria that do not correspond to any combinations mentioned for the cachexia stages.

Appendix D - Edmonton Symptom Assessment System

Centre universitaire de santé McGill — McGill University Health Centre

☐ HME MCH ☒ HGM MGH ☒ HRV RVH
☒ HNM MNH ☐ ITM MCI ☐ CL LC

Échelle revisée d'évaluation des symptômes d'Edmonton (EESE r)
Revised Version Edmonton Symptom Assessment System (ESAS r)

Veuillez écrire lisiblement en lettres moulées / Please type of print legibly

Nom / *Name*	Date	AAYY	MM	JD

Pour chaque item suivant, encerclez le chiffre que décrit mieux votre état de santé au cours des DERNIÈRES 24 HEURES
For each of the following items, please circle the number that best describes your health DURING the LAST 24 HOURS

Aucune douleur *No pain*										**La pire douleur possible** *Worst possible pain*
0	1	2	3	4	5	6	7	8	9	10
Aucune fatigue (fatigue=manque d'énergie) *No tiredness (tiredness=lack of energy)*										**La pire fatigue possible** *Worst possible tiredness*
0	1	2	3	4	5	6	7	8	9	10
Aucune nausée (nausée=envie de vomir) *No nausea*										**La pire nausée possible** *Worst possible nausea*
0	1	2	3	4	5	6	7	8	9	10
Aucune dépression (dépression=tristesse) *No depression (depression=feeling sad)*										**La pire dépression possible** *Worst possible depression*
0	1	2	3	4	5	6	7	8	9	10
Aucune anxiété (anxiété=se sentir nerveux) *No anxiety (anxiety=feeling nervous)*										**La pire anxiété possible** *Worst possible anxiety*
0	1	2	3	4	5	6	7	8	9	10
Aucune somnolence (somnolence=se sentir endormi) *No drowsiness (drowsiness=feeling sleepy)*										**La pire somnolence possible** *Worst possible drowsiness*
0	1	2	3	4	5	6	7	8	9	10
Aucun manque d'appétit *No lack of appetite*										**Le pire manque d'appétit possible** *Worst possible lack of appetite*
0	1	2	3	4	5	6	7	8	9	10
Meilleure sensation de bien-être (bien-être=comment vous vous sentez en général) *Best wellbeing (wellbeing=how you feel overall)*										**Aucune sensation de bien-être** *Worst possible wellbeing*
0	1	2	3	4	5	6	7	8	9	10
Aucun essoufflement *No shortness of breath*										**Le pire essoufflement possible** *Worst possible shortness of breath*
0	1	2	3	4	5	6	7	8	9	10
Aucun(e) autre problème *No other problem*						(par exemple constipation) *(for example constipation)*				**Le pire possible** *Worst possible*
0	1	2	3	4	5	6	7	8	9	10

Signature du patient / *Patient's Signature*

DM-2310 (REV 2015/05/21) CUSM repro MUHC

Appendix E – Abridged-Scored Patient-Generated Subjective Global Assessment

Centre universitaire de santé McGill — McGill University Health Centre

☐ HME *MCH* ☒ MGH *HGM* ☐ HRV *RVH*
☐ HNM *MNH* ☐ ITM *MCI* ☐ CL *LC*

* F M U – 0 5 0 9 *

Autoévaluation nutritionnelle globale subjective - Version abréviée (ANGS)

Abridged-Scored patient-generated subjective global assessment (PG-SGA)

Numéro de dossier / Unit Number / Nom du patient / Patient's Name

1. Poids (voir la feuile de travail 1) / *Weight (see worksheet 1)* — Section 1

Résumé de mon poids actuel et récent / *Summary of my current and recent weight* (Encercler / *Circle* (kg) / *lbs* (meters) / *ft*)

Actuellement, je pèse environ *I currently weigh about* _____ kg / lbs	**Il y a six mois je pesais environ** *Six months ago I weighed about* _____ kg / lbs
Je mesure environ *I am about* _____ metres / ft	**Au cours des deux dernières semaines, mon poids :** *During the past two weeks, my weight has :*
Il y a un mois, je pesais environ *One month ago, I weighed about* _____ kg / lbs	☐ **Est resté stable (0)** *Has not changed (0)* ☐ **A augmenté (0)** *Has increased (0)* ☐ **A diminué (1)** *Has decreased (1)*

2. Apport alimentaire / *Food Intake* — Section 2

Par rapport à ce que je mange d'habitude, je dirais que la quantité de nourriture que j'ai consommé le mois dernier est :
As compared to my normal intake, I would rate my food intake during the past month as :

☐ **Inchangée (0)** *Unchanged (0)* ☐ **Plus grande (0)** *More than usual (0)* ☐ **Plus petite (1)** *Less than usual (1)*

Maintenant, je mange : *I am now taking :*

☐ **De la nourriture normale, mais moins que d'habitude (1)** *Normal food but less than normal amount (1)*	☐ **Uniquement des suppléments nutritionnels (3)** *Only nutritional supplements (3)*
☐ **Peu de nourriture solide (2)** *Little solid food (2)*	☐ **Très peu de choses (4)** *Very little of anything (4)*
☐ **Seulement des liquides (3)** *Only liquids (3)*	☐ **Seulement par alimentation par sonde ou voie i.v. (0)** *Only tube feedings or onlly nutrition by vein (0)*

3. Symptômes / *Symptoms* — Section 3

Au cours des deux dernières semaines, les problèmes suivants m'ont empêché(e) de manger suffisament (cochez touts les cases qui s'appliquent):
I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply) :

☐ **Aucune difficulté à manger (0)** *No problems eating (0)*	☐ **Les aliments ont un drôle/n'ont plus de goût (1)** *Things taste funny or have no taste (1)*	☐ **Bouche sèche (1)** *Dry mouth (1)*
☐ **Pas d'appétit, pas envie de manger (3)** *No appetite, just did not feel like eating (3)*	☐ **Difficulté à avaler (2)** *Problems swallowing (2)*	☐ **Les aliments ont une odeur désagréable (1)** *Smells bother me (1)*
☐ **Nausées (1)** *Nausea (1)*	☐ **Vomissements (3)** *Vomiting (3)*	☐ **Impression de satiété (1)** *Feel full quickly (1)*
☐ **Constipation (1)** *Constipation (1)*	☐ **Diarrhée (3)** *Diarrhea (3)*	
☐ **Présence d'ulcères buccaux (2)** *Mouth sores (2)*	☐ **Fatigue (1)** *Fatigue (1)*	

☐ **Douleur; précisez à quel endroit (3) :** *Pain; Where ? (3) :*

☐ **Other* (1) (par exemple: dépression, manque d'argent, problèmes de dents) :** *Other* (1) (for example: depression, money, or dental problems) :*

4. Capacités fonctionelles / *Activities and Functioning* — Section 4

Voici dans quelle mesure j'ai pu accomplir mes activités habituelles durant le mois dernier :
Over the past month, I would generally rate my activity as :

☐ **Capable d'accomplir mes activités habituelles, sans restriction (0)** *Normal with no limitations (0)*

☐ **Capable d'accomplir mes activités habituelles, mais avec restrictions (1)** *Not my normal self, but able to be up and about with fairly normal activities (1)*

☐ **Incapable d'accomplir la plupart de mes activités habituelles, et ai passé moins de la moitié des journées au lit ou au fauteuil (2)** *Not feeling up to most things but in bed or chair less than half the day (2)*

☐ **Capable d'accomplir très peu de mes activités habituelles et ai passé a plus partie de mes journées au lit ou au fauteuil (3)** *Able to do little activity and spend most of the day in bed our chair (3)*

☐ **Ai dû passer presque tout mon temps au lit, ne me levant que très rarement (3)** *Pretty much bedridden, rarely out of bed (3)*

5. Score cumulatif pour les sections 1 à 4 : / *Additive Score of Sections 1-4 :* ☐ A

Signature / *Signature*

Date et heure / *Date and time* A A Y Y / M M / J D 00:00

Appendix F – Pages from Participant's Logbook

Resistance Log Book

	Date							
Exercises								
Sit to Stand	Reps							
	Sets							
Seated Chest Press	Reps							
	Sets							
	Elastic							
Seated Row	Reps							
	Sets							
	Elastic							
Calf Raises	Reps							
	Sets							
	Elastic							
Bicep Curl	Reps							
	Sets							
	Elastic							

*Borg scale value_____

Cardio Log Book

Exercise (walk, cycle)	Date	Time	Borg Scale*

*Write down the appropriate number from the Borg Scale

Appendix G – Baseline Questionnaire (Expectations Questionnaire)

Participant Identification Number _____

Expectation questionnaire

Answer each of the following questions.

1) On a scale of **1-10,** how **active** do you perceive yourself as?

Not active at all Very Active

1 2 3 4 5 6 7 8 9 10

2) On a scale of **1-10** how **deconditioned** (or "out of shape") do you think you are?

Very Fit Very Deconditioned

1 2 3 4 5 6 7 8 9 10

3) Do you feel exercise prescription or consultations with a kinesiologist (specialized personal trainer) could benefit you?

Yes No

4) What do you expect or hope to gain from an exercise program specially designed for cancer patients?

_____

_____

Appendix H – Exit Survey (Satisfaction Questionnaire)

Participant Identification Number _____

Satisfaction Questionnaire

Answer each of the following questions.

1) How well do you feel you tolerated the exercise program?

Cannot tolerate				Easily tolerated
1	2	3	4	5

2) For what reasons did you miss any of your exercise sessions? (select all that apply)

a. No time / Too busy
b. Fatigue
c. Pain or other symptoms (i.e. nausea, depression, vertigo)
d. Too difficult
e. Other (please specify):_____

3) On average, how motivated were you to complete each exercise session?

No motivation			Very motivated	
1	2	3	4	5

4) Do you feel that the exercise program increased your functionality in your every day life?

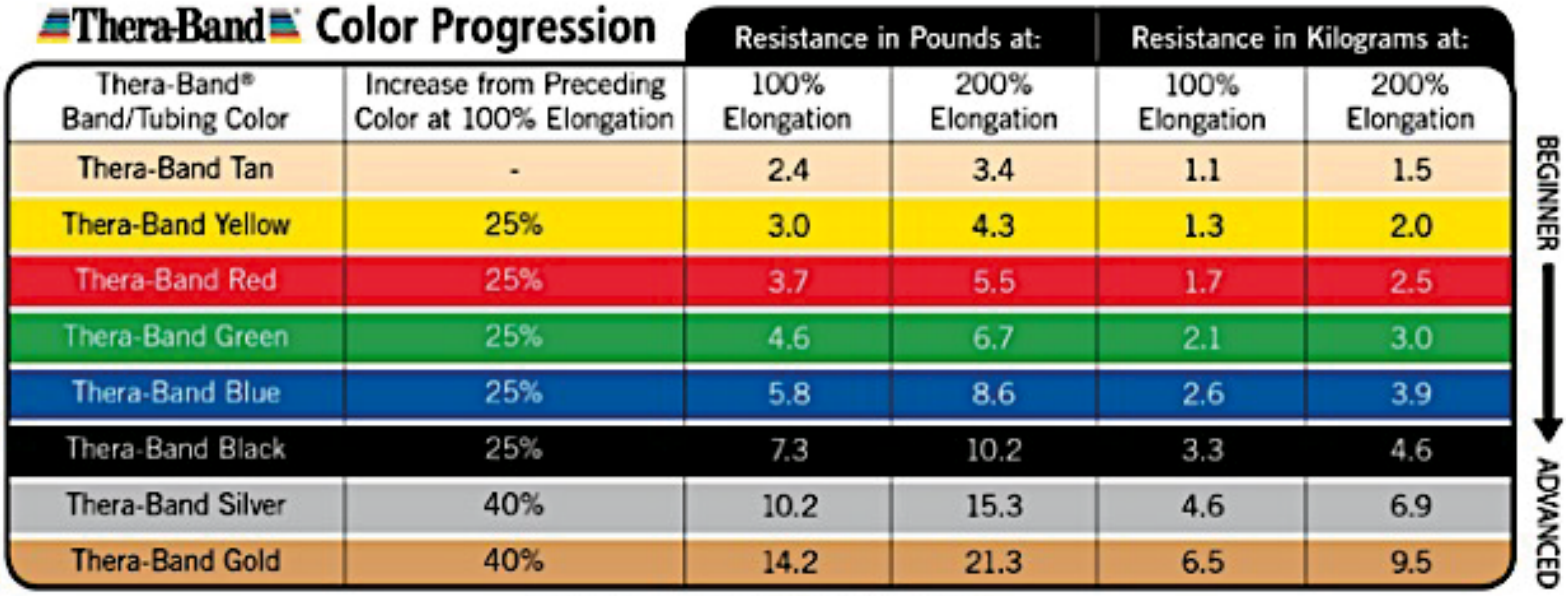
Not at all				Very much so
1	2	3	4	5

5) Did you enjoy participating in the program?

Not at all				Very much so
1	2	3	4	5

6) Can you think of any changes that can better the exercise program for you?

Appendix I – Theraband™ Color Progression Chart



Thera-Band Color Progression

Thera-Band® Band/Tubing Color	Increase from Preceding Color at 100% Elongation	Resistance in Pounds at: 100% Elongation	Resistance in Pounds at: 200% Elongation	Resistance in Kilograms at: 100% Elongation	Resistance in Kilograms at: 200% Elongation
Thera-Band Tan	-	2.4	3.4	1.1	1.5
Thera-Band Yellow	25%	3.0	4.3	1.3	2.0
Thera-Band Red	25%	3.7	5.5	1.7	2.5
Thera-Band Green	25%	4.6	6.7	2.1	3.0
Thera-Band Blue	25%	5.8	8.6	2.6	3.9
Thera-Band Black	25%	7.3	10.2	3.3	4.6
Thera-Band Silver	40%	10.2	15.3	4.6	6.9
Thera-Band Gold	40%	14.2	21.3	6.5	9.5

BEGINNER → ADVANCED

weight rather than Therabands™ (Sit-to-Stand & calf raises). Different colors represent a different resistance and are listed from the least to the most resistance in **Figures 3, 4 and 5** (yellow, red, green, and blue). In terms of most commonly used resistance bands, the majority of participants reported using the red band (90.5%, n=19) at least once, at some point throughout the program. The second most frequently used color was the green band, and was used by 76% (n=16) of participants, at least once, at some point during the study. Because each color-band corresponds to a resistance in kilograms at 100% elongation, we were able to quantify the group's total resistance for every exercise, every week, and view their overall progression. To view color bands' associated resistance in kilograms at 100% elongation see Appendix I or refer to legend of **Figures 3, 4 and 5**. Represented in **Figures 3, 4 and 5** below, you will see the number of participants that reported using each color band, every week. In addition, under each week is the total calculated resistance for the group (in kg) and the corresponding collective percent increase in resistance from the previous week. Lastly, the overall percent progression is bolded under each figure and ranged between 21-29% increase between weeks 1 and 4. Paired t-tests between resistances used in week 1 and week 4, show that strength progression for the chest press (1.64 ±0.29 vs. 1.98 ±0.32 kgs; $p<0.001$), seated row (1.66 ±0.24 vs. 2.06 ±0.32 kgs; $p<0.001$), and bicep curl (1.55 ±0.23 vs. 2.0 ±0.28 kgs; $p<0.001$) was significantly increased over time.

Figure 3

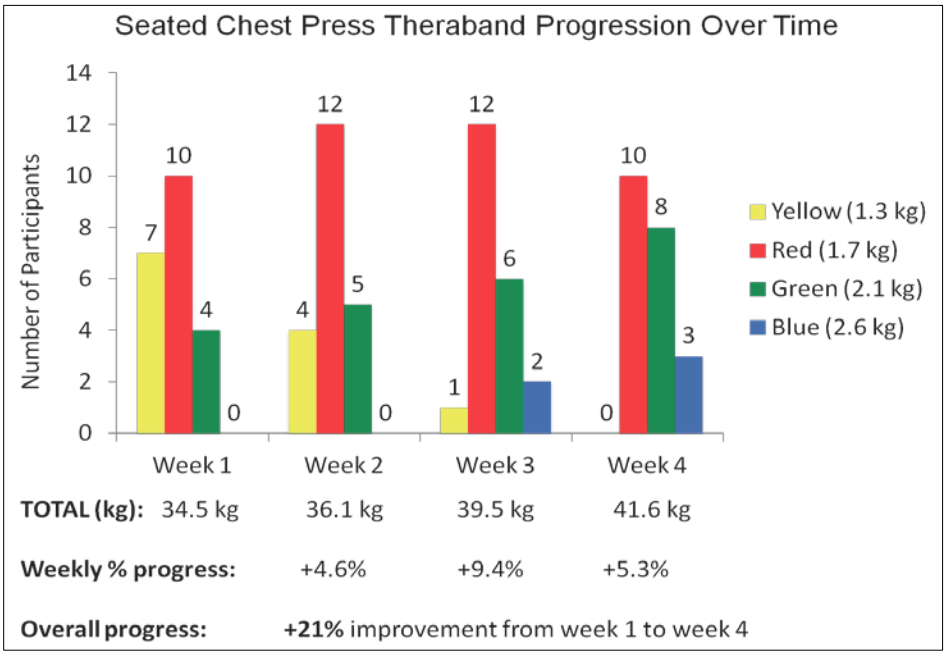


Figure 4

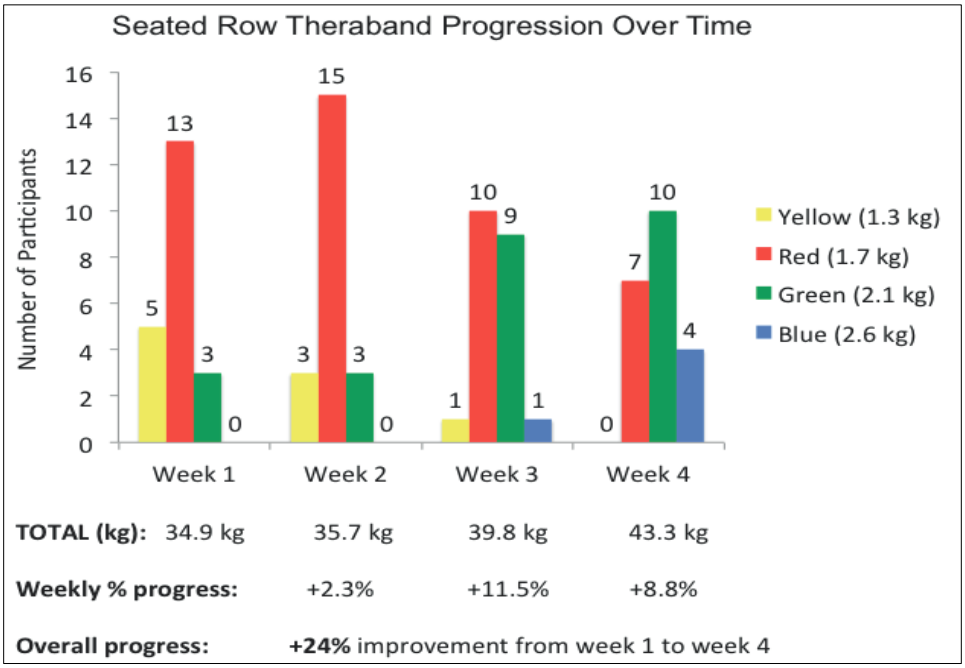
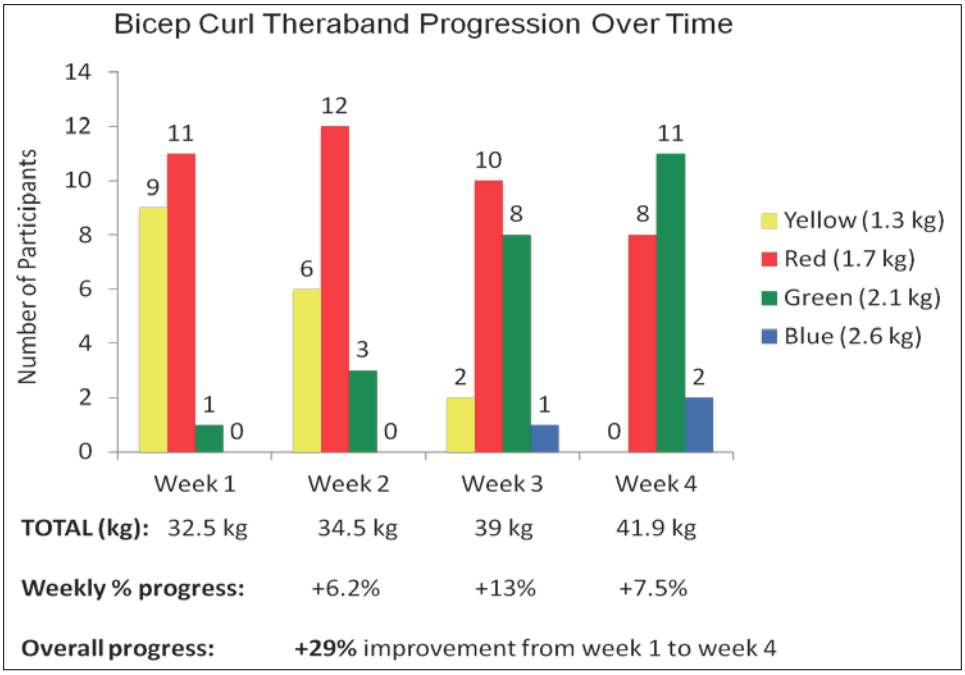
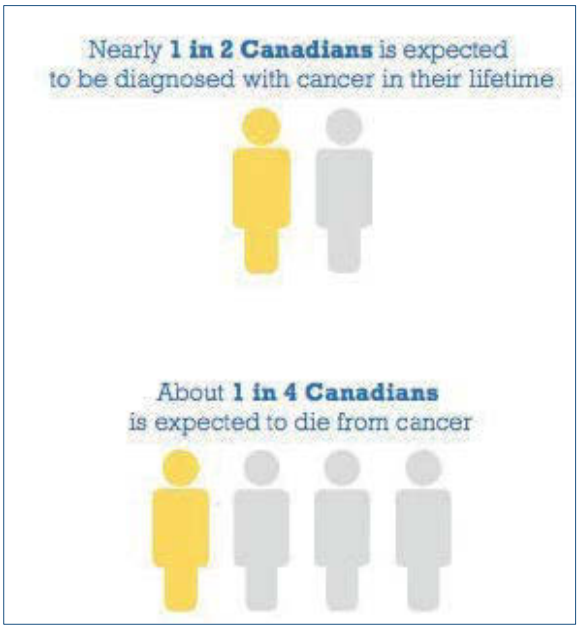


Figure 5

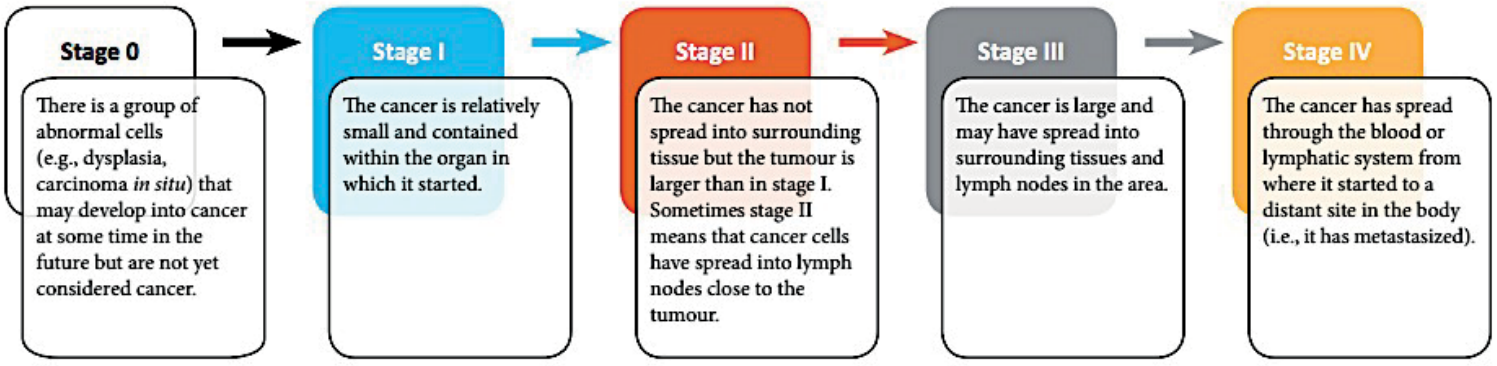


Appendix A – Canadian Cancer Statistics (2018)



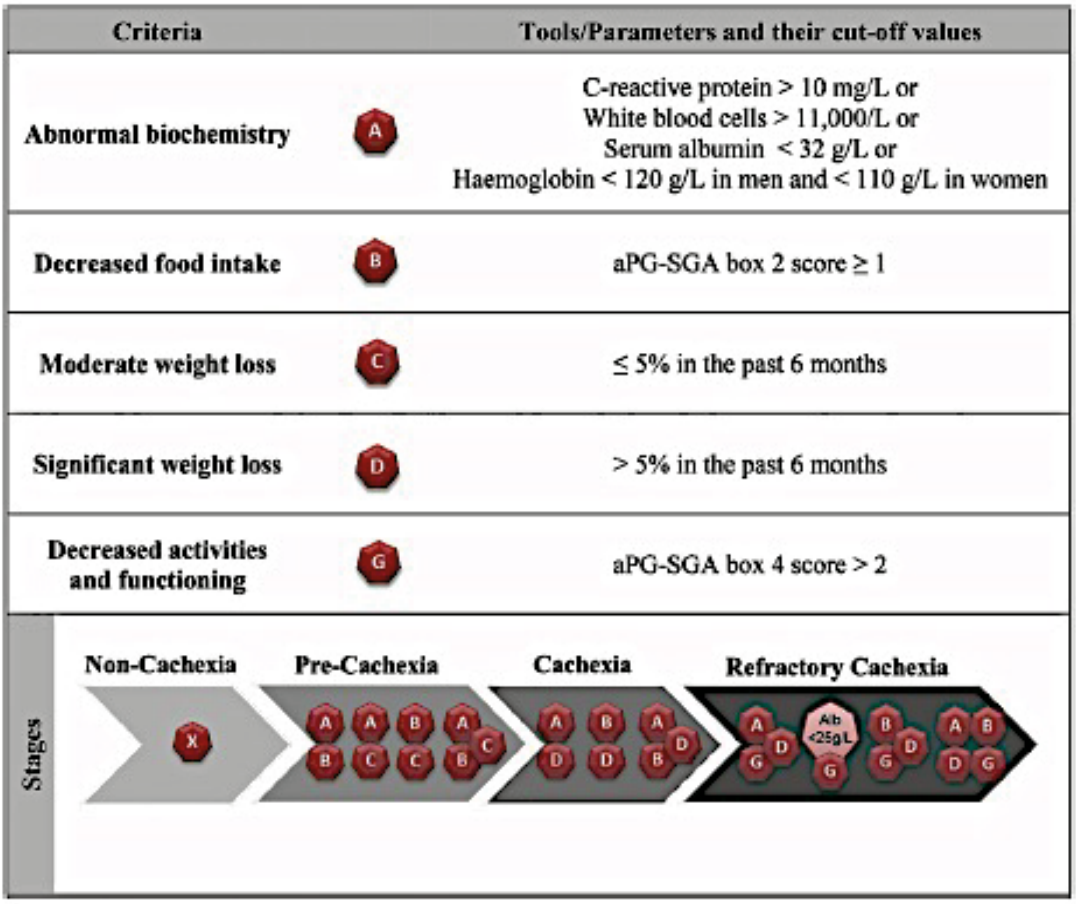
Appendix B – Cancer "TNM" Staging System

Canadian Cancer Society (2018)



Sometimes uppercase letters are added to the number to divide these categories into substages.

Appendix C – Vigano et al. (2016) Cancer Cachexia Classification System



aPG-SGA: abridged Patient-Generated Subjective Global Assessment
(box 2 – food intake; box 4 – activities and functioning); X: insufficient number of criteria or criteria that do not correspond to any combinations mentioned for the cachexia stages.

Appendix D - Edmonton Symptom Assessment System

Centre universitaire de santé McGill — McGill University Health Centre

☐ HME MCH ☒ HGM MGH ☒ HRV RVH
☒ HNM MNH ☐ ITM MCI ☐ CL LC

Échelle revisée d'évaluation des symptômes d'Edmonton (EESE r)
Revised Version Edmonton Symptom Assessment System (ESAS r)

Veuillez écrire lisiblement en lettres moulées / Please type of print legibly

Nom / *Name*	Date	AAYY	MM	JD

Pour chaque item suivant, encerclez le chiffre que décrit mieux votre état de santé au cours des DERNIÈRES 24 HEURES
For each of the following items, please circle the number that best describes your health DURING the LAST 24 HOURS

Aucune douleur *No pain*	0	1	2	3	4	5	6	7	8	9	10 **La pire douleur possible** *Worst possible pain*
Aucune fatigue (fatigue=manque d'énergie) *No tiredness (tiredness=lack of energy)*	0	1	2	3	4	5	6	7	8	9	10 **La pire fatigue possible** *Worst possible tiredness*
Aucune nausée (nausée=envie de vomir) *No nausea*	0	1	2	3	4	5	6	7	8	9	10 **La pire nausée possible** *Worst possible nausea*
Aucune dépression (dépression=tristesse) *No depression (depression=feeling sad)*	0	1	2	3	4	5	6	7	8	9	10 **La pire dépression possible** *Worst possible depression*
Aucune anxiété (anxiété=se sentir nerveux) *No anxiety (anxiety=feeling nervous)*	0	1	2	3	4	5	6	7	8	9	10 **La pire anxiété possible** *Worst possible anxiety*
Aucune somnolence (somnolence=se sentir endormi) *No drowsiness (drowsiness=feeling sleepy)*	0	1	2	3	4	5	6	7	8	9	10 **La pire somnolence possible** *Worst possible drowsiness*
Aucun manque d'appétit *No lack of appetite*	0	1	2	3	4	5	6	7	8	9	10 **Le pire manque d'appétit possible** *Worst possible lack of appetite*
Meilleure sensation de bien-être (bien-être=comment vous vous sentez en général) *Best wellbeing (wellbeing=how you feel overall)*	0	1	2	3	4	5	6	7	8	9	10 **Aucune sensation de bien-être** *Worst possible wellbeing*
Aucun essoufflement *No shortness of breath*	0	1	2	3	4	5	6	7	8	9	10 **Le pire essoufflement possible** *Worst possible shortness of breath*
Aucun(e) autre problème *No other problem*	0	1	2	3	4	5	6	7	8	9	10 _____ (par exemple constipation) *(for example constipation)* **Le pire possible** *Worst possible*

Signature du patient / *Patient's Signature*

DM-2310 (REV 2015/05/21) CUSM repro MUHC

Appendix E – Abridged-Scored Patient-Generated Subjective Global Assessment

Centre universitaire de santé McGill — McGill University Health Centre

☐ HME *MCH* ☒ MGH *HGM* ☐ HRV *RVH*
☐ HNM *MNH* ☐ ITM *MCI* ☐ CL *LC*

* F M U – 0 5 0 9 *

Autoévaluation nutritionnelle globale subjective - Version abréviée (ANGS)

Abridged-Scored patient-generated subjective global assessment (PG-SGA)

Numéro de dossier / Unit Number / Nom du patient / Patient's Name

1. Poids (voir la feuile de travail 1) / *Weight (see worksheet 1)* — Section 1

Résumé de mon poids actuel et récent / *Summary of my current and recent weight* (Encercler / *Circle* (kg) / *lbs* (meters) / *ft*)

Actuellement, je pèse environ *I currently weigh about* _____ kg / lbs	**Il y a six mois je pesais environ** *Six months ago I weighed about* _____ kg / lbs
Je mesure environ *I am about* _____ metres / ft	**Au cours des deux dernières semaines, mon poids :** *During the past two weeks, my weight has :*
Il y a un mois, je pesais environ *One month ago, I weighed about* _____ kg / lbs	☐ **Est resté stable (0)** *Has not changed (0)* ☐ **A augmenté (0)** *Has increased (0)* ☐ **A diminué (1)** *Has decreased (1)*

2. Apport alimentaire / *Food Intake* — Section 2

Par rapport à ce que je mange d'habitude, je dirais que la quantité de nourriture que j'ai consommé le mois dernier est :
As compared to my normal intake, I would rate my food intake during the past month as :

☐ **Inchangée (0)** *Unchanged (0)* ☐ **Plus grande (0)** *More than usual (0)* ☐ **Plus petite (1)** *Less than usual (1)*

Maintenant, je mange : *I am now taking :*

☐ **De la nourriture normale, mais moins que d'habitude (1)** *Normal food but less than normal amount (1)*	☐ **Uniquement des suppléments nutritionnels (3)** *Only nutritional supplements (3)*
☐ **Peu de nourriture solide (2)** *Little solid food (2)*	☐ **Très peu de choses (4)** *Very little of anything (4)*
☐ **Seulement des liquides (3)** *Only liquids (3)*	☐ **Seulement par alimentation par sonde ou voie i.v. (0)** *Only tube feedings or onlly nutrition by vein (0)*

3. Symptômes / *Symptoms* — Section 3

Au cours des deux dernières semaines, les problèmes suivants m'ont empêché(e) de manger suffisament (cochez touts les cases qui s'appliquent):
I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply) :

☐ **Aucune difficulté à manger (0)** *No problems eating (0)*	☐ **Les aliments ont un drôle/n'ont plus de goût (1)** *Things taste funny or have no taste (1)*	☐ **Bouche sèche (1)** *Dry mouth (1)*
☐ **Pas d'appétit, pas envie de manger (3)** *No appetite, just did not feel like eating (3)*	☐ **Difficulté à avaler (2)** *Problems swallowing (2)*	☐ **Les aliments ont une odeur désagréable (1)** *Smells bother me (1)*
☐ **Nausées (1)** *Nausea (1)*	☐ **Vomissements (3)** *Vomiting (3)*	☐ **Impression de satiété (1)** *Feel full quickly (1)*
☐ **Constipation (1)** *Constipation (1)*	☐ **Diarrhée (3)** *Diarrhea (3)*	
☐ **Présence d'ulcères buccaux (2)** *Mouth sores (2)*	☐ **Fatigue (1)** *Fatigue (1)*	

☐ **Douleur; précisez à quel endroit (3) :** *Pain; Where ? (3) :*

☐ **Other* (1) (par exemple: dépression, manque d'argent, problèmes de dents) :** *Other* (1) (for example: depression, money, or dental problems) :*

4. Capacités fonctionelles / *Activities and Functioning* — Section 4

Voici dans quelle mesure j'ai pu accomplir mes activités habituelles durant le mois dernier :
Over the past month, I would generally rate my activity as :

☐ **Capable d'accomplir mes activités habituelles, sans restriction (0)** *Normal with no limitations (0)*

☐ **Capable d'accomplir mes activités habituelles, mais avec restrictions (1)** *Not my normal self, but able to be up and about with fairly normal activities (1)*

☐ **Incapable d'accomplir la plupart de mes activités habituelles, et ai passé moins de la moitié des journées au lit ou au fauteuil (2)** *Not feeling up to most things but in bed or chair less than half the day (2)*

☐ **Capable d'accomplir très peu de mes activités habituelles et ai passé a plus partie de mes journées au lit ou au fauteuil (3)** *Able to do little activity and spend most of the day in bed our chair (3)*

☐ **Ai dû passer presque tout mon temps au lit, ne me levant que très rarement (3)** *Pretty much bedridden, rarely out of bed (3)*

5. Score cumulatif pour les sections 1 à 4 : / *Additive Score of Sections 1-4 :* ☐ A

Signature / *Signature*

Date et heure / *Date and time* A A Y Y / M M / J D 00:00

Appendix F – Pages from Participant's Logbook

Resistance Log Book

	Date							
Exercises								
Sit to Stand	Reps							
	Sets							
Seated Chest Press	Reps							
	Sets							
	Elastic							
Seated Row	Reps							
	Sets							
	Elastic							
Calf Raises	Reps							
	Sets							
	Elastic							
Bicep Curl	Reps							
	Sets							
	Elastic							

*Borg scale value_____

Cardio Log Book

Exercise (walk, cycle)	Date	Time	Borg Scale*

*Write down the appropriate number from the Borg Scale

Appendix G – Baseline Questionnaire (Expectations Questionnaire)

Participant Identification Number _____

Expectation questionnaire

Answer each of the following questions.

1) On a scale of **1-10,** how **active** do you perceive yourself as?

Not active at all Very Active

1 2 3 4 5 6 7 8 9 10

2) On a scale of **1-10** how **deconditioned** (or "out of shape") do you think you are?

Very Fit Very Deconditioned

1 2 3 4 5 6 7 8 9 10

3) Do you feel exercise prescription or consultations with a kinesiologist (specialized personal trainer) could benefit you?

Yes No

4) What do you expect or hope to gain from an exercise program specially designed for cancer patients?

_____

_____

Appendix H – Exit Survey (Satisfaction Questionnaire)

Participant Identification Number _____

Satisfaction Questionnaire

Answer each of the following questions.

1) How well do you feel you tolerated the exercise program?

Cannot tolerate				Easily tolerated
1	2	3	4	5

2) For what reasons did you miss any of your exercise sessions? (select all that apply)

a. No time / Too busy
b. Fatigue
c. Pain or other symptoms (i.e. nausea, depression, vertigo)
d. Too difficult
e. Other (please specify):_____

3) On average, how motivated were you to complete each exercise session?

No motivation			Very motivated	
1	2	3	4	5

4) Do you feel that the exercise program increased your functionality in your every day life?

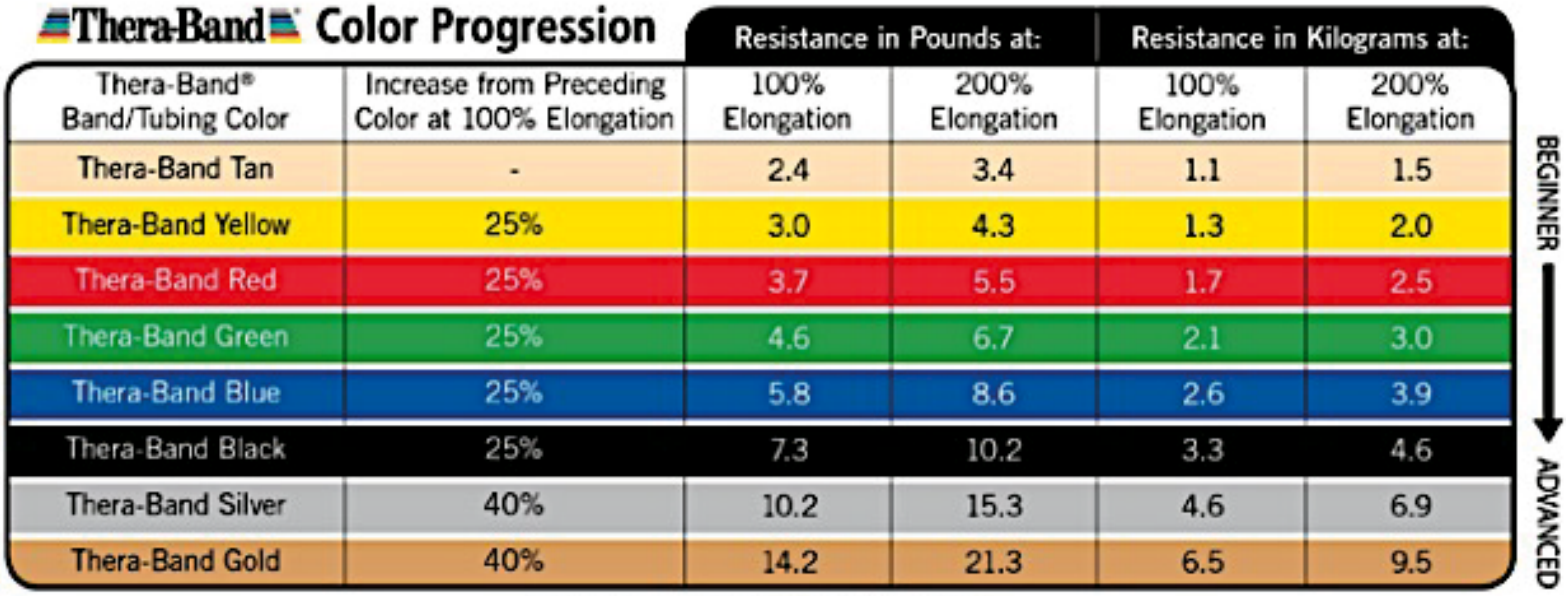
Not at all				Very much so
1	2	3	4	5

5) Did you enjoy participating in the program?

Not at all				Very much so
1	2	3	4	5

6) Can you think of any changes that can better the exercise program for you?

Appendix I – Theraband™ Color Progression Chart



Thera-Band Color Progression

Thera-Band® Band/Tubing Color	Increase from Preceding Color at 100% Elongation	Resistance in Pounds at: 100% Elongation	Resistance in Pounds at: 200% Elongation	Resistance in Kilograms at: 100% Elongation	Resistance in Kilograms at: 200% Elongation
Thera-Band Tan	-	2.4	3.4	1.1	1.5
Thera-Band Yellow	25%	3.0	4.3	1.3	2.0
Thera-Band Red	25%	3.7	5.5	1.7	2.5
Thera-Band Green	25%	4.6	6.7	2.1	3.0
Thera-Band Blue	25%	5.8	8.6	2.6	3.9
Thera-Band Black	25%	7.3	10.2	3.3	4.6
Thera-Band Silver	40%	10.2	15.3	4.6	6.9
Thera-Band Gold	40%	14.2	21.3	6.5	9.5

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