The Feasibility and Acceptability of a Virtually-Supported Home Exercise Program for People with Multiple Myeloma

by

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ABSTRACT

Introduction: Exercise could help alleviate the significant morbidity experienced by people with multiple myeloma (MM). It is unclear if current cancer-specific exercise guidelines are appropriate for this unique population. Supervision, tailoring, and flexibility are proposed as key program elements in this population, but no studies to date have evaluated the acceptability of an intervention that employs these components.

Objectives: The purpose of this study was to determine the feasibility and acceptability of a 12-week tailored virtually-supported home exercise program for people with MM that progresses towards the 2019 Exercise Guidelines for Cancer Survivors.

Methods: A single group multi-method pre/post feasibility study was conducted. The program involved live group classes, independent home workouts, and additional aerobic exercise. Prescriptions were progressed as recommended by the 2019 Exercise Guidelines for Cancer Survivors. Participants completed a virtual fitness assessment and questionnaires at baseline (BL) and week 12 (12WK). Based on a qualitative description method, a sub-set of participants completed one-on-one interviews after the exercise program.

Data Analysis: Feasibility measures were analyzed descriptively. Secondary effectiveness outcomes were analyzed using either a Wilcoxon Signed Rank Test (if distribution not normal) or a Paired t-test (if distribution normal). A team of four coders analyzed transcripts from qualitative interviews using content analysis.

Results: 29 participants consented and 26 completed all follow-up testing (89.7%). Participants completed 89.9% of live group classes, 82.7% of independent home workouts, and 89.7% of independent aerobic exercise. No serious adverse events (grade ≥ 3) occurred in the study. Minor

adverse events related to the intervention included grade 1 back pain (n=2), grade 2 back pain (n=1), and grade 2/3 back pain (n=1). One compression fracture unrelated to the intervention occurred during the study. Quality of life (FACT-MM) significantly improved (BL: 111±23 vs 12WK: 118±19, p=0.0332). Thirty-second sit-to-stand score significantly improved (BL: 13.1±4.5 repetitions vs 12WK: 15.8±4.3 repetitions, p<0.0001). Plank duration significantly improved (BL: 78.3±46.0 seconds vs 12WK: 119.9±73.4 seconds, p=0.0002). Timed single leg stance significantly improved (BL: 23.1±13.3 seconds vs 12WK: 31.8±12.6 seconds, p=0.0002). 20 participants completed the post-program interviews. Three themes emerged related to program strengths/limitations: *One Size Does Not Fit All*, *App Usability*, and *Sustainability*. *One Size Does Not Fit All* contained two sub-themes: *Supportive and Responsive Programming* and *Diverse Exercise Opportunities*.

Conclusion: The 12-week virtually-supported home exercise program was feasible and acceptable but associated with a higher than anticipated rate of musculoskeletal events. Tailoring, supervision, active support, knowledgeable and empathetic personnel, multiple delivery formats, and a user-friendly eHealth application appear to be key components in facilitating feasibility and acceptability. The findings from this study warrant further investigation with a larger scale, randomized controlled trial. Future studies should continue to work with people with MM as partners to create sustainable programs that meet the needs and priorities of the patient population.

PREFACE

This thesis is an original work by Graeme Macdonald Purdy. The research project(s) of which this thesis is a part, received research ethics approval from the Health Research Ethics Board of Alberta: Cancer Committee. Project name " Feasibility of a Virtually Supported Home-Based Resistance and Aerobic Exercise Program for Cancer Survivors with Multiple Myeloma", No. HREBA-CC-20-0201, August 26th, 2020.

Chapter 3 of this thesis is in the process of being published as G.M. Purdy, C.P. Venner, P. Tandon, M.L. McNeely, "Feasibility of a tailored and virtually-supported home exercise program for people with multiple myeloma using a novel exercise application". Co-authors listed have contributed to either: i.) conception or design of work [GP, CV, PT, MM], ii.) acquisition, analysis, or interpretation of data for the work [GP, CV, PT, MM], or iii.) drafting the work or revising it critically for important intellectual content [GP, CV, PT, MM]. All persons listed have read and approved the final version of the manuscript.

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DEDICATION

This thesis is dedicated to the myeloma community. I'm forever grateful to those of you who put your trust in me and volunteered to participate in the studies that make up this thesis. Getting to know you and work alongside you was the most rewarding part of this experience, so from the bottom of my heart, thank you all.

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DEFINITIONS AND ABBREVIATIONS

Cancer Related

Multiple myeloma (MM): a cancer that forms in a type of white blood cell called plasma cells. The disease causes abnormal (cancerous) plasma cells to accumulate in the bone marrow, crowding out healthy blood cells (1).

Relapse: A deterioration after a period of improvement (2).

Recurrence: When a cancer returns after the disease is non-detectable for a period of time.

Refractory: A cancer is said to be refractory when it does not respond to treatment. It may be resistant at the beginning of treatment, or it may become resistant during treatment.

Treatment Related

Chemotherapy: a systemic therapy that aims to target cancerous myeloma cells in the body. Treatment involves the use of chemical agents to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing (1).

Stem cell transplantation (SCT): a treatment commonly used for multiple myeloma where a patient's own stem cells (autologous) are removed, stored, then given back to the patient following high dose chemotherapy (1).

Targeted therapy: a systemic therapy that uses drugs to target specific molecules or proteins on or inside cancer cells that send signals to the cells to grow or divide. By targeting these molecules, the drugs stop the growth and spread of cancer cells and limit the harm done to healthy cells. Types of targeted therapy drugs include proteosome inhibitors, immunomodulating drugs, and monoclonal antibodies (1).

Radiation therapy: this treatment applies beams of ionizing radiation to affected areas to induce apoptosis in myeloma cells, reducing tumor size. Radiation therapy is used to manage isolated plasmacytomas, bone pain related to medullary plasmacytomas and osteolytic lesions, and for preventing paralysis in patients with disease-related spinal cord compression (1).

Vertebroplasty: a spinal stabilization procedure that involves the injection of medical grade cement (polymethyl methacrylate) into a vertebral column fracture (3).

Kyphoplasty: a spinal stabilization procedure that involves the inflation of a balloon followed by injection of medical grade cement (polymethyl methacrylate) into a vertebral compression fracture (3).

Disease & Treatment Sequelae

Myopathy: a disease of the muscle in which muscle fibers do not function properly. In the case of myeloma, this is often caused by the prolonged used of corticosteroids like dexamethasone (steroid-induced myopathy), which leads to muscle breakdown and weakness, particularly in proximal muscles (4).

Peripheral neuropathy: a progressive condition involving the injury or degeneration of the peripheral nerves caused by neurotoxic systemic therapies. Symptoms include pain, numbness, tingling, and hyper-sensitivity to cold in the hands and feet (2).

Bone lesion: Build-up of cancerous plasma cells in bone marrow leads to breakdown of bone, leading to bone lesions, or areas where bones are thin and weak, or even hollow. Lesions can be focal or lytic. Focal lesions are early, abnormal areas in the bone marrow that can progress into lytic lesions. Lytic lesions are areas where bone has been destroyed, leaving a hole in the bone, which can lead to fractures (2).

Osteolytic bone destruction: the process of bone breakdown or destruction brought on by the pathophysiology associated with multiple myeloma where osteoclast (cells that breakdown bone) (2).

Anemia: a condition in which the body lacks enough red blood cells to carry an adequate supply of oxygen to the body's tissues (2).

Dyspnea: the feeling of shortness of breath. This is a side-effect from some myeloma treatments, including bortezomib and lenalidomide.

Outcomes Related

ESAS: Edmonton Symptom Assessment Scale. This is a self-reported tool used to determine the burden a patient is experiencing as it relates to a variety of common symptoms and side-effects from cancer and cancer treatment.

FACT-MM: Functional Assessment of Cancer Therapy – Multiple Myeloma. This is a quality of life measure part of the FACIT system specific to the multiple myeloma population.

FACIT-Fatigue: Functional Assessment of Chronic Illness Therapy – Fatigue. This is a 13-item patient-reported instrument that assesses self-reported fatigue and its impact upon daily activities and function.

FACT/GOG-NTX4: Functional Assessment of Cancer Therapy/Gynecologic Oncology Group – Neurotoxicity 4 Item Questionnaire. This is a self-reported instrument that provides a targeted assessment of symptoms of peripheral neuropathy in both the hands and feet.

FACT-Bone Pain: Functional Assessment of Cancer Therapy – Bone Pain. This is a self-reported instrument part of the FACIT system that is used to assess cancer-related bone pain and its effects on patient quality of life.

Study Related

MY PROGRESS: Myeloma Progressive Resistance and Aerobic Exercise Study. This is the study that forms the basis of chapters 3 and 4 of this thesis.

HEAL-Me: Healthy Eating, Active Living, and Mindful Energy. This is the web-based application that was used to deliver MY PROGRESS.

CHAPTER 1: INTRODUCTION

1.1 Brief Introduction

Cancer is currently the leading cause of death in Canada, with an estimated 83,300 deaths from cancer occurring in Canada in 2020 (5). Multiple myeloma (MM) is a plasma cell cancer that accounts for roughly 1% of cancer diagnoses and 13% of hematologic cancers. With a 5-year survival of approximately 45% and a 10-year survival of approximately 30%, MM has a low survival rate relative to the cancer population as a whole (5). MM is a cancer that causes osteolytic bone destruction (6), leading to deformities, pain, reduced mobility and functioning, fatigue, and fracture risk (7). For perspective, up to 70% of people with MM experience vertebral fracture (8) leading to vertebral collapse and loss of several inches in height. Further, pathological changes in the bone impair muscle function (9). Treatment advances in the past few decades have led to patients living longer (10). However, common treatments including chemotherapy and stem cell transplantation have lasting, debilitating side-effects, including fatigue, myopathy, neuropathy, and pain (11). It's clear that supportive care services are needed to improve patient function in the face of this lasting symptom burden (12).

Exercise improves physical function and recent evidence-informed exercise guidelines have been released for people living with cancer (13). Guidelines suggest that regular exercise is beneficial for managing cancer-related impairments, including fatigue, quality of life, and physical function. Unfortunately, the guidelines are primarily based on randomized controlled trials in breast and prostate cancer. Given the unique pathophysiology and treatment regimen for MM, these guidelines are likely not appropriate. Looking to original research, there is a paucity of exercise trials (14) with some studies showing promise in outcomes including strength, fatigue, and aerobic capacity (15-17), and others reporting non-significant effects from exercise (18-22). Overall, more research is required to determine what levels and kinds of exercise are appropriate for people with MM.

1.2 Problem Statement and Purpose of the Thesis

The proposed study seeks to advance the care of people with MM by testing the feasibility and acceptability of a virtually-supported home exercise program for people with MM. Evidence on the feasibility and benefits of exercise in MM is mixed, with some research

reporting positive effects (15-17), and other studies reporting non-significant results (18-22). Further, key methodological flaws in these studies have limited the effectiveness, generalizability, and reproducibility of the interventions employed. The proposed study will address these flaws by employing a virtually supported home-based exercise program using a novel exercise application for chronic disease to leverage the benefits of home exercise programming (flexibility and convenience) with the benefits of in-person programming (direct supervision and program tailoring) in a representative group of people with MM. The proposed thesis is a two-part, multi-method study evaluating a single group pre- post-intervention study of a virtually supported home-based exercise program for people with MM. The overall purpose of this study is to assess the feasibility and acceptability of a MM-specific exercise intervention progressing individuals with MM to the 2019 Exercise Guidelines for Cancer Survivors.

1.3 Objectives

Quantitative Component (Chapter 3): To determine the feasibility of a 12-week virtually supported home-based aerobic and resistance exercise program that aims to progress individuals to the 2019 Exercise Guidelines for Cancer Survivors in a sample of people with multiple myeloma, as defined by:

- Recruitment rate: ≥ 21 participants consenting to the study over a 7-month recruitment period (primary endpoint)
- Completion rate: ≥ 80% of participants consenting to the study complete the 12-week assessment
- Safety: the absence of serious adverse events (≥ grade 3) related to the intervention
- Adherence: average completion of ≥ 75% of the exercise prescription amongst participants

Qualitative Component (Chapter 4): To determine the acceptability of the program, defined by: (i) participants' perceptions of the virtually-supported home exercise program and application, and (ii) participants' perceptions of the strengths and limitation of the exercise program and application.

Secondary Objective: To determine the preliminary efficacy of the intervention by assessing changes in leg strength (30-second sit-to-stand), core strength (plank endurance test), balance (single leg balance test), and quality of life (FACT-MM).

1.4 Hypothesis

Primary Hypothesis: The 12-week virtually supported home exercise program will prove feasible and acceptable for people with MM.

Secondary Hypothesis: The 12-week virtually-supported home exercise program will demonstrate preliminary efficacy with significant improvements in physical function and quality of life.

CHAPTER 2: LITERATURE REVIEW

2.1 Multiple Myeloma

Multiple myeloma (MM) is an incurable cancer characterized by proliferation of malignant monoclonal plasma cells in the bone marrow (23). The disease has a median age of diagnosis of roughly 70 (24); 37% of patients are <65 years, 26% are 65-74, and 37% are >75. Multiple myeloma is thought to arise most commonly from monoclonal gammopathy of undetermined clinical significance, which progresses to smouldering myeloma, and finally, to symptomatic myeloma (25). This process of progression is driven by a series of genetic abnormalities that underlie the multistep pathogenesis of MM (23). MM is diagnosed using a combination of detailed medical history and physical examination, routine laboratory testing, bone marrow examination, and radiographic imaging (26). Multiple myeloma can be diagnosed when clonal bone marrow plasma cells are ≥10% or by the presence of biopsy-proven bony or extramedullary plasmacytoma and any one of the following myeloma-defining events (27):

- Evidence of end organ damage attributable to the plasma cell proliferative disorder (27):
  - Hypercalcemia
  - Renal insufficiency
  - Anemia
  - Bone lesions
- Any one of the following markers of malignancy (27):
  - Clonal bone marrow plasma cell percentage ≥60%
  - Involved: uninvolved serum free light chain ratio ≥100
  - >1 focal lesion(s) on MRI study

MM is staged according to the International Staging System, which defines three risk groups based on serum β_2-microglobulin and albumin levels, chromosomal abnormalities, and serum lactate dehydrogenase levels (28). Briefly, the greater the β_2-microglobulin level, the lower the albumin level, the greater the number of chromosomal abnormalities, and the higher the serum lactate dehydrogenase levels, the higher the stage, or the poorer the prognosis.

MM accounts for roughly 1% of cancer diagnoses and 13% of hematologic cancers. With a 5-year survival of approximately 45% and a 10-year survival of approximately 30%, MM has a

low survival rate relative to the cancer population as a whole (5). Individuals with MM experience osteolytic bone destruction (6) due to the production of abnormal light-chain proteins, which serve as cytokines that suppress osteoblasts (cells that build bone) and stimulate osteoclasts (cells that break down bone) (23). For context, bony lesions develop in almost 80% of patients with newly diagnosed MM (29), and up to 70% of patients experience vertebral fracture (8), leading to vertebral collapse and the loss of several inches in height (30). Indeed, 58% of patients report experiencing bone pain (29). Further, MM leads to anemia, which is present in approximately 73% of patients at diagnosis (31), which is generally related to myeloma cells infiltrating bone marrow or renal dysfunction. Indeed, renal impairment is present in 20-40% of cases at initial diagnosis (29). This is most often the result of direct tubular damage from excess light chain protein load, which can be compounded by dehydration, hypercalcemia (high calcium levels in the blood), and the use of nephrotoxic medications, like antibiotics and anti-inflammatories (32). Lastly, pathological changes in the bone microenvironment at bony lesion sites can impair muscle function, leading to loss of muscle strength and/or muscle mass (9). This is a cytokine-mediated process that occurs through bone-muscle cross-talk (33) and IL-6 is thought to play an important role. Taken together, the pathological sequelae of MM lead to persistent deformities, chronic pain, reduced mobility and functioning, fatigue, risk of infection, and a risk of future fracture (7).

2.2 Multiple Myeloma Treatment

With improved treatments for cancer, cancer deaths have declined by 27% over the past decade (34). In the case of MM, new treatment regimens have extended median survival from roughly 3 years to 6 years over the past two decades (35, 36). In fact, in patients eligible for autologous stem cell transplantation, it is now expected their median overall survival will be 10 years (37, 38). For young patients with MM, the goal of therapy is to achieve the deepest possible response and to maintain that response for as long as possible. For elderly patients, the goal is to minimize symptoms and maximize response with as little toxicity as possible. Currently, in Alberta, standard care treatment (39) can be grouped into those who are transplant-eligible and those who are transplant-ineligible.

For patients who are transplant-eligible, treatment begins with an induction regimen. Patients receive 4-6 28-day cycles of cyclophosphamide, bortezomib, and dexamethasone

weekly. A twice-weekly schedule can be used for sicker patients requiring a more rapid initial response. Patients can also receive 4-6 28-day cycles of a different protocol, which replaces cyclophosphamide with lenalidomide daily for 21 days. A 21-day schedule is available for sicker patients requiring a more rapid initial response. This regimen was recently approved for provincial funding. Alternatively, patients may receive the doublet of lenalidomide and dexamethasone (40). Those with high risk myeloma, as indicated by high risk cytogenetic aberrations (including 13q deletion, t(4;14)(p16;q32) chromosomal translocation, 17p deletion, and absence of hyperdiploidy), should be considered for clinical trials. In the absence of clinical trials, patients receive similar treatment to the protocols described above. Side-effects from induction regimens relevant to physical function include fatigue (bortezomib, lenalidomide), myopathy (bortezomib, dexamethasone), generalized weakness (bortezomib, dexamethasone, lenalidomide), muscle cramps (bortezomib, lenalidomide), joint, muscle, and/or bone pain (bortezomib, dexamethasone, lenalidomide), peripheral neuropathy (bortezomib), dyspnea (bortezomib, lenalidomide), peripheral edema (lenalidomide), low blood counts (cyclophosphamide, bortezomib, lenalidomide), dizziness (bortezomib, dexamethasone, lenalidomide), and changes in affect (dexamethasone) (41-44).

Mobilization follows induction, using cyclophosphamide with granulocyte-colony stimulating factor (G-CSF) to stimulate granulocyte production and stem cell release into the bloodstream. Relevant side-effects from mobilization include weakness (G-CSF), bone and joint pain (G-CSF), peripheral edema (G-CSF), and low blood counts (cyclophosphamide) (43, 45). The stem cells are then collected using a process known as leukapheresis, frozen, and stored for later use. Immediately prior to transplantation, a high-dose conditioning regimen of melphalan is administered. Relevant side-effects from conditioning include low blood counts (melphalan) (46). The stem cells are then thawed and infused back into the patient. Following transplantation, patients may receive consolidation therapy: 2 cycles of bortezomib, lenalidomide, and dexamethasone if they fail to achieve a deep response or have high risk cytogenetics. Following consolidation, all patients then receive lenalidomide daily for 21-28/28 days every 4 weeks until disease progression. Those with high-risk disease may also receive bortezomib every 2 weeks for 2 years (maintenance therapy).

For patients who are transplant-ineligible, 9-12 cycles of cyclophosphamide, bortezomib, and dexamethasone is recommended. Alternatively, a regimen of lenalidomide daily for 21/28 days and dexamethasone weekly until progression is now routinely used. This approach is an oral regimen, is well tolerated, and is effective (40). Following initial therapy, all patients should receive maintenance therapy with bortezomib every 2 weeks for 2 years. Elderly, frail, very elderly (>75 years of age), and those with significant co-morbidities are at increased risk of toxicity. It is recommended that dose reductions be considered for patients with ≥ 1 of those risk factors. Median survival amongst transplant-ineligible patients is around 5 years (47)

Unfortunately, given the progressive nature of MM, relapse is expected. For those who have had a disease-free interval of > 2 years, a 2nd high dose chemotherapy treatment with autologous stem cell transplantation can be used. However, most patients will not be candidates for a second transplant. For these patients, current regimens often involve the anti-CD38 monoclonal antibody daratumumab combined with either lenalidomide or bortezomib (and dexamethasone). Alternatively, patients may receive carfilzomib-based regimens, including carfilzomib, lenalidomide and dexamethasone or carfilzomib and dexamethasone. Finally, patients may receive pomalidomide in combination with dexamethasone if refractory to both lenalidomide and bortezomib. Relevant side-effects from daratumumab and carfilzomib include edema (carfilzomib, daratumumab, pomalidomide), backache or musculoskeletal pain (carfilzomib, daratumumab, pomalidomide), fatigue (carfilzomib, daratumumab, pomalidomide), dizziness (daratumumab, pomalidomide), GI symptoms (pomalidomide), neuropathy (daratumumab, pomalidomide), dyspnea (pomalidomide), and low cell counts (carfilzomib) (48-50).

Beyond the above practices, additional supportive therapies are often indicated including bisphosphonates, vertebroplasty or kyphoplasty, orthopedic surgery, and radiation therapy. Bisphosphonates are a class of drug that bind to the surface of bone to slow bone resorption. They increase bone density, thus reducing vertebral fractures, skeletal related events, and pain (51). It is recommended that people with MM take either pamidronate or zoledronate every 4 weeks for 2 years (39). If after 2 years, the patient has achieved remission and is in the stable plateau phase of treatment, the bisphosphonates can be discontinued. If the MM still requires active treatment, bisphosphonate treatments continue but are decreased in frequency to every 3

months. Unfortunately, bisphosphonates increase risk of developing osteonecrosis of the jaw, with a 4-11.4% incidence (51). Additional side effects include fatigue, joint, muscle, and bone pain, generalized weakness, dizziness, and dyspnea (52, 53).

Vertebroplasty and balloon kyphoplasty are procedures indicated following vertebral compression fracture. Vertebroplasty involves the injection of medical grade cement (polymethyl methacrylate) and is designed to stabilize the fracture and reduce pain. Balloon kyphoplasty involves the inflation of a balloon followed by injection of polymethyl methacrylate into the fracture (54). This procedure stabilizes the vertebrae, restores vertebral height, and can reduce both kyphotic deformity and pain. In addition, orthopedic surgeries involving pinning for impending or actual bone fractures (long bone or vertebral column) are used in MM to stabilize the spinal column. Although surgeries like these can improve pain and overall function, they can also lead to stiffness/tightness throughout the back. Finally, radiation therapy is used to manage isolated plasmacytomas, bone pain related to medullary plasmacytomas and osteolytic lesions, and for preventing paralysis in patients with disease-related spinal cord compression. Radiation therapy applies beams of ionizing radiation to an affected area to induce apoptosis in myeloma cells and reduce tumor size (55). The resulting effect is decompression of nerves and pressure sensors (55, 56) with complete or partial pain relief with or soon after treatment. In addition, radiation therapy induces re-calcification in radiated bone, reducing the risk of fractures (56), but also leads to fatigue.

Taken together, people with MM have a complex and lengthy treatment journey. Each stage of treatment is associated with significant side effects including, but not limited to weakness, myopathy, pain, neuropathy, fatigue, and shortness of breath (57-59). These side effects have implications for the maintenance of both quality of life and physical function. Furthermore, these treatment side effects compound with the disease-related morbidities mentioned earlier (i.e., pain, reduced physical functioning, fatigue, and risk of fracture), making the lived experience of people with MM even more challenging. Overall, due to improved treatments extending disease survival, people with MM may be living longer, but with a significant and lasting symptom burden.

2.3 Exercise in Cancer

Supportive care services have the potential to improve patient function and quality of life in the face of this lasting symptom burden (12). Rehabilitation has been proposed as a measure to improve quality of life and functioning in light of the increased prevalence of chronic diseases amongst an already ageing population (60). Historically, cancer patients were told to avoid physical activity, but research throughout the 1990s and 2000s challenged this advice. Recent evidence-informed exercise guidelines have been released for people living with cancer (13). The 2019 Exercise Guidelines for Cancer Survivors recommend people living with cancer engage in moderate-intensity aerobic training ≥ 3x/week, in ≥ 30 minutes sessions, for ≥ 8-12 weeks. They should also engage in resistance training ≥ 2x/week, using ≥ 2 sets of 8-15 repetitions, at an intensity of ≥ 60% of one repetition maximum. The 2019 Guidelines highlight that there is strong evidence on the benefits of regular exercise for anxiety, depressive symptoms, fatigue, health-related quality of life, lymphedema, and physical function. There is moderate evidence on the benefits of regular exercise for bone health and sleep. Lastly, there is insufficient evidence on the benefits of regular exercise for cardiotoxicity, chemotherapy-induced peripheral neuropathy, cognitive function, falls, nausea, pain, sexual function, and treatment tolerance.

It's important to note that there are several limitations to these guidelines. First, the majority of available evidence involves the most common cancers, including early stage breast cancer and prostate cancers. This limits the generalizability of results to other cancer populations, including MM. Indeed, the guidelines acknowledge that there is little information regarding the feasibility, safety, or benefits of exercise in individuals living with advanced cancer. Some individuals may not be able to adequately or safely exercise at the levels recommended in the guidelines. Given the unique pathophysiology and treatment regimen for MM, it is a group for which these guidelines may not be appropriate. Indeed, the guidelines acknowledge their recommendations may not be safe for people with bone fragility. As such, specifically tailored exercise prescriptions may be needed for this unique population.

2.4 Exercise in Multiple Myeloma

There is a paucity of exercise trials in MM, with studies presenting mixed results (14). One of the earliest exercise interventions in MM was conducted by Coleman et al. in 2003 (18).

The study was a randomized controlled trial (intervention group: n=14, control group: n=10) with a primary aim of feasibility. Participants (mean age: 55.9 years; 58% male) included those not at high risk for pathologic fracture who were transplant-eligible and were currently receiving high-dose chemotherapy during induction treatment. The intervention group completed home-based exercise combining strength resistance training and aerobic training. The aerobic component involved fast paced walking at a moderate intensity, while the strength component involved a series of roughly 6 exercises, completed ~2 sets of 8 repetitions. Additional information regarding frequency, intensity, and duration were not described. Overall, the study found that the exercise group increased lean body weight, compared to the control group. No significant differences were found in terms of muscle strength, aerobic capacity, fatigue, mood disturbance scores, and sleep quality. Adverse events were not reported in this study. Furthermore, researchers observed a high attrition rate (42%) and, in a separate publication, reported that participants completed the six-month exercise prescription 75% of the time (61). The authors reported that exclusion criteria, phone support, easy to use equipment, motivation, and providing exercise modifications facilitated adherence. Overall, this study had a poorly described exercise intervention and delivered a home-based program that was possibly underdosed and under-adhered to, leading to non-significant results. Further, by not reporting on adverse events, the safety of the intervention remains unclear.

The same research group published a second randomized controlled trial in 2008 (19). 135 participants (66 in exercise group and 69 in control group) who were eligible for intensive treatment and tandem transplant without high risk of fracture or spinal cord compression nor recent history of anemia requiring blood transfusions were enrolled in the study (mean age: 55 years; 58% male). The intervention included erythropoietin administration and a home-based exercise program involving stretching, aerobics, and strength resistance training. The initial intervention was 15 weeks long, but 69 participants continued into a long-term participation arm that extended the intervention to 30 weeks. Outcomes included attempts and duration of stem cell collection, number of transfusions, time-to-recovery after transplantation, response to intensive therapy, and aerobic capacity (six-minute walk test). The aerobic component involved walking to tolerance (until tired), while the strength resistance training was performed on alternate days, including biceps curls, triceps extensions, chair stands, and hamstring curls. No

additional prescription parameters were provided. The authors found no significant differences in aerobic capacity, response to intensive treatment or number of transfusions between groups. However, fewer attempts at stem cell collection occurred in the exercise group compared with the control group. Further, several serious adverse events were reported, including lower extremity deep vein thrombosis (n=12), upper extremity deep vein thrombosis (n=17), pulmonary embolism (n=5), as well fever, hyponatremia, pneumonia, hyperglycemia, infection, and neutropenia. The researchers speculate the clotting-related adverse events were related to thalidomide and erythropoietin use. The researchers reported an 11% attrition rate but did not report adherence rates to the exercise prescription. Overall, this study also had a poorly described unsupervised intervention and yielded non-significant results.

Coleman et al. completed a third randomized controlled trial in 2012 (20) with the same inclusion/exclusion criteria as their 2008 study, this time with 187 participants not at risk of fracture or compression (mean age: 56 years; 58% male) who were taking prophylactic erythropoietin (95 in exercise group, 92 in control group). The intervention was a 15-week home-based exercise program and involved daily stretching exercises, as well as strength resistance training (biceps curls, triceps extensions, chair stands, and hamstring strengthening) and aerobic walking for an undescribed duration on alternating days. Strength training was prescribed at a moderate intensity (60-80% of 1RM), but it's unclear how the researchers were able to prescribe exercise as % 1RM in a home program. Aerobic walking was performed at a moderate intensity (65-80% of age-predicted maximum heart rate, Borg 11-13). Study outcomes included objectively-measured sleep quality, fatigue, and aerobic capacity (6-Minute Walk Test). No statistically significant differences in sleep quality, fatigue, or aerobic capacity were observed between groups. Adverse events are not reported in this study. The authors reported that 4 participants didn't exercise at all, while 22 participants completed more than what was prescribed. No other adherence data are reported, but completion rates were 89%. Overall, it's unclear what the total dosage and adherence to this home-program was and the non-significant results suggest this program was not effective. It's also unclear whether the intervention was safe, given adverse events were not reported.

Knols et al. conducted a randomized controlled trial assessing the effects of an outpatient exercise program on patients recovering from stem-cell transplantation (n=131; mean age: 46.7

years; 59% male) (15). 28% of participants had MM. Participants were recruited between 3 weeks and 6 months following transplantation and were excluded if they had painful joints, unstable osteolysis, chronic pain, lesions in the nervous system, or uncontrolled comorbidities. The 12-week supervised intervention involved both endurance and resistance training, 2x/week in a physiotherapy practice or fitness center near the participant's home. Aerobic exercise was performed at a moderate intensity for at least 20 minutes each session. The whole-body resistance training was performed using dumbbells, but no details around the prescription parameters are discussed. Primary outcomes included knee extension strength, grip strength, walking speed, and 6-minute walk test. Secondary measures included body composition, quantified walking activity, self-reported physical activity, fatigue, and health-related quality of life. Completion rates were 87% and attendance rates were 85%. Results showed improvements in knee extension strength, walking speed, 6-minue walk distance, and physical function-related quality of life, when compared to the control group. However, no improvements in grip strength, body composition, quantified walking activity, self-reported physical activity, fatigue, or other health-related quality of life domains (role, cognitive, social, fatigue, pain, insomnia) were observed when compared to the control group. The researchers reported that no adverse events occurred during the study. This study showed promising results for some aspects of physical function and fitness, but it's unclear why no significant changes in physical activity, fatigue, and health-related quality of life were observed. Furthermore, the exclusion criteria employed in this study severely limit the generalizability of results to the myeloma population.

Groeneveldt and colleagues completed a single-group feasibility-focused exercise intervention in 2013 (16). The study included those with a MM diagnosis without spinal instability or risk of fracture, regardless of current treatment status (n=37; mean age: 61 years; 58% male). The primary objective was feasibility, with secondary outcomes of fatigue, cardiorespiratory fitness, body composition, and muscle strength. The intervention was 6 months long and involved stretching, aerobic, and resistance training 3x/week. Aerobic training started at 15-minute bouts of 50% heart rate reserve (low-moderate intensity) and progressed by either 5 minutes or 5% heart rate reserve every 4 weeks. The final goal was 30 minutes of aerobic exercise at 60% heart-rate reserve (moderate intensity) in the last 4 weeks of the program. The resistance training was individually tailored to target the major muscle groups in the lower and

upper body using elastic bands, weightlifting equipment, or body weight. Participants started at 3 sets of 10 repetitions, progressed to 3 sets of 15 repetitions, then increased the weight and returned to 3 sets of 10. This process was repeated incrementally throughout the intervention. Exercise was completed 1x/week in a group personal training format and 2x/week self-directed at home for the first 3 months, then 1x/month in the supervised format and 3x/week at home for the next 3 months. Results included: recruitment (80% of eligible participants consented, 82% of consented passed screening, 76% of those who passed screening enrolled); attendance (87% for group sessions, 86% for home-program in first 3 months, 73% for home-program in from month 4-6); completion rates (100% for 3-month test, 76% for 6-month test). The study also found improvements in fatigue, upper limb strength, and lower limb strength at 3 and 6 months but no change in aerobic capacity or body composition. The researchers reported that no adverse events occurred during the study. Overall, this study reported improvements in some key outcomes but reports non-significant improvements in other key outcomes like aerobic fitness. This may be due to the heavy reliance on unsupervised/unsupported exercise. It's also unclear what participant adherence was to the intensity and volume within exercise sessions.

Shallwani and colleagues conducted a retrospective analysis of people with MM who participated in the Hope & Cope Rehabilitation and Exercise Oncology Program in Montreal, Canada (62). The program offers low-moderate intensity aerobic exercise for 15-60 minutes daily and low-moderate intensity resistance training 2-3x/week, with participants choosing either supervised or home-based programming, based on preference. All participants (n=41; mean age: 61 years; 73% male) in this program were receiving chemotherapy at the time of initial evaluation. Outcomes included adherence, self-report physical activity levels, and fatigue scores. Follow-up testing was performed at a median of 6 weeks after baseline. Participants increased their self-reported level of physical activity and reduced fatigue. The researchers did not report on adverse events. Adherence was 70.7%. Factors associated with non-adherence included history of pathological fracture, history of radiation to bone, and history of spinal cord compression. Participants reported pain, fatigue, and decreased motivation as barriers to adherence. Overall, while this intervention was associated with a reduction in fatigue, the poor adherence and the reported exercise barriers suggest that the program was not tolerated well.

More recently, a research group from the Netherlands published a series of articles stemming from their randomized controlled trial: the EXIST Study (21, 22, 63-65). The EXIST Study involved 109 participants (54 in exercise group, 55 in control group; median age: 53.5 years; 63% male). Participants included those with MM (53%) and those with non-Hodgkin's lymphoma (47%). Participants were enrolled either during first line treatment (if MM diagnosis) or during first relapse (if lymphoma diagnosis) and were sufficiently recovered from an allogenic stem cell transplantation 6-12 weeks prior. Participants with extensive osteolytic lesions with risk of fracture, severe comorbid conditions, or progressed disease were excluded. The 18-week high-intensity supervised intervention involved aerobic and resistance exercise for 60 minutes 2x/week for weeks 1-12 and 60 minutes for 1x/week for weeks 13-18. The aerobic component was completed in interval format, consisting of two eight-minute cycling bouts (one before the resistance component and one after). Intervals were 30s work, 60s rest at the start, but progressed to 30s work, 30s rest. The resistance exercise component followed the same frequency as the aerobic component and involved 2 sets of 10 repetitions at 65-80% 1RM for 12 weeks, then 2 sets of 20 repetitions at 35-40% 1RM for the last 6 weeks. Exercises included four standardized exercises (vertical row, leg press, chest press, and flies) and two additional exercises for the abdominals and upper legs. The intervention also included 6 counselling sessions. Short-term outcomes included aerobic fitness, muscular fitness, and fatigue. The study reported completion rates (85%) and attendance rates (86%) but found no statistically significant differences in aerobic fitness, muscular fitness, or fatigue between groups. Eight serious adverse events were reported in this study, 4 in each group. The authors state that none of the events were related to study participation. However, 1 participant experienced a calf strain during a training session but recovered from the injury within the intervention period. Furthermore, a long-term effectiveness and cost-effectiveness follow-up was completed after 1-year (64). This analysis reported no differences in long-term effectiveness outcomes, with those in the exercise group having higher secondary costs but lower informal care costs when compared to the control group. The exercise intervention was not cost-effective from a societal perspective. The authors speculate that the non-significant results are attributable to poor exercise adherence, suboptimal timing of intervention, or contamination in the control group, but data from the process evaluation suggest that adherence to the exercise prescription was sufficient (22).

Recently, Larsen and colleagues published an interim feasibility analysis of the first 30 participants from a currently on-going randomized controlled trial evaluating the efficacy of supervised and home-based physical exercise in patients newly diagnosed with MM (66). Participants (mean age: 68 years; 77% men) included those without unstable fracture or cardiac failure. The attending hematologist determined preliminary exercise restrictions. The 10-week intervention involves exercise 3x/week, supervised by a physiotherapist ~1x/week (8 times in total over the intervention) or unsupervised at home. Sessions included a 5-minute warm-up (RPE 10-11), 20 minutes of aerobic exercise (RPE 12-13, progressing to 14-16), and 30-45 minutes of strengthening exercises, involving 3 sets of 12-15 repetitions with a progression to 3 sets of 10-12 repetitions at a higher resistance. Strengthening exercises included five exercises for the lower extremity (knee extension, knee flexion, hip extension, toe raising, and chair stands), three exercises for the upper extremity (frontal raise, elbow extension, elbow flexion), and one exercise for the trunk (modified deadbug). Exercise restrictions followed the principles by Galvao and colleagues, wherein participants do not use weights in strengthening exercises for involved sites and movements are restricted at the involved site (67). Participants were also instructed to be independently active for 30 minutes/day on the other 4 days of the week. Primary outcomes from the interim analysis included feasibility of the intervention and the test protocols (static knee extension, 30s sit to stand, grip strength, 6-minute walk test). 82% of screened patients were eligible, 75% of eligible patients enrolled, and 20% of enrolled participants dropped out after inclusion. Adherence (attendance) to supervised sessions was 99%, 89% for home-based sessions. 94% of participants completed activity on the recommended number of days. All tests were tolerated and safe, with relatively small rates of non-completions (<15%). Two adverse events occurred in this study (one case of dizziness, one case of pain) both resulting in the discontinuation of the supervised session that was being completed when the event occurred. This trial is currently still accruing, so effectiveness outcomes are not yet published.

The most recent study in this population is a phase 2 randomized trial following up Groeneveldt's feasibility trial, the MASCOT trial (68). Participants with stable disease who had completed initial treatment or were on maintenance therapy and had ECOG scores of 0-2 were eligible. The study used an adapted Zelen study design to randomize participants while avoiding

contamination bias (randomization ratio of 3:1). The intervention replicated the details for Groeneveldt's feasibility trial (16). The primary outcome for this study was fatigue (FACIT-F), while secondary outcomes included quality of life (FACT-G and Hospital Anxiety and Depression Scale), cardiorespiratory fitness (VO2peak), lower limb muscle strength (10-repetition max and leg extension test) hand grip strength, and physical activity (Actigraph). Body composition was also assessed using bioelectrical impedance. 51 participants accepted to be in the intervention group (median age: 64 years, 55% male). The majority of participants had bone disease. Retention was high (88%), attendance was fair (75%). Results showed no change in fatigue, cardiorespiratory fitness, or physical activity, but a significant improvement in leg strength was observed. Interestingly, exploratory analyses showed that those with clinical fatigue were able to significantly improve their fatigue in the intervention group, when compared to the control group. No serious adverse events were reported. There was one reported case of hip pain and four reported cases of lower back pain, but the authors state that it was unclear if they were related to the intervention. Overall, this controlled study presented a safe program that was well tolerated but found non-significant effects in most outcomes.

2.5 Patient Perceptions & Preferences of Exercise in Myeloma

In addition to the exercise trials described above, a number of qualitative and quantitative studies have been conducted to explore the perspectives of people with MM towards exercise and physical activity. In general, people with MM experience declines in physical activity after diagnosis, with activity levels typically reaching their lowest when on treatment (69-71). Cross-sectional surveys have found that less than 20% of people with MM meet guideline exercise recommendations (69, 70, 72), with factors related to non-participation including fatigue, injuries, pain, lack of knowledge on safety, fear of injury, and fear of infection (70, 71, 73). Despite these barriers, they have indicated an interest in exercise programming (69, 70) with a preference for a combination of aerobic and resistance exercise performed at a light- to moderate-intensity (73). A qualitative study by Craike et al. highlights a patient-identified need for individualization, flexibility, and supervision of exercise programming in myeloma (73). These findings are supported by a recent quantitative survey conducted by Nicol and colleagues, which found that people with MM prefer exercise programming with flexible times, locations close to home, and direct supervision from an exercise professional with cancer-specific training

(69). Given these findings, it has been proposed that program tailoring and supervision might be necessary to facilitate both increased participation in, and benefits from exercise programming for people with MM (74). Offering flexible program options that meet participants' needs is likely also key.

2.6 Summary and Rationale

Overall, the limited exercise studies available in MM present mixed results, and the feasibility and effectiveness of the interventions investigated in the literature remain unclear. While some studies show promise in outcomes including strength, fatigue, and aerobic capacity (15-17), most studies have reported non-significant effects from exercise (18-22). Indeed, several limitations are identifiable in the literature. Several interventions, particularly home-based interventions, appear to have underdosed exercise interventions (19, 20), which possibly explains their non-significant results. In addition, home exercise programming does not typically contain the supervision and tailoring that patients desire (69, 73). However, highly supervised in-person programs are not always flexible and convenient for patients, which are also program characteristics identified by patients as important (69, 73). Additionally, many of the currently available studies in this population lack detail on exercise prescriptions (18, 75), which limits the reproducibility of protocols to confirm or refute the reported results. Understandably so, fear of fracture, pain, and infection (70) has created apprehension towards exercise amongst both clinicians and people with MM. It's possible that this perspective has restricted participants, clinicians, and exercise specialist from delivering an appropriate dose of exercise for participants. Indeed, despite expressing a desire for exercise support, less than 20% of people with MM are meeting exercise guidelines (72). At the very least, some level of tailoring is likely required to ensure programming can be both safe and effective. Unfortunately, limited information on tailoring practices specific to MM can be gleaned from the literature, as most studies have described their prescriptions in minimal detail. More research is required to determine what levels and kind of exercise are most appropriate for people with MM and how programming can be adapted to the MM population in order to maintain exercise tolerance. We believe that an optimal program design for this population involves leveraging the benefits of in-person programming (supervision and tailoring) with the benefits of home programming (flexibility and convenience).

CHAPTER 3: FEASIBILITY OF A TAILORED AND VIRTUALLY-SUPPORTED HOME EXERCISE PROGRAM FOR PEOPLE WITH MULTIPLE MYELOMA USING A NOVEL EXERCISE APPLICATION

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3.1 ABSTRACT

Introduction: Exercise could help alleviate the significant morbidity experienced by people with multiple myeloma (MM). It is unclear if current exercise guidelines are appropriate for this unique population. The purpose of this study was to determine the feasibility and preliminary efficacy of a 12-week home exercise program progressing people with MM to current exercise guidelines.

Methods: A single group pre/post feasibility study was conducted. Participants completed a tailored 12-week virtually-supported home exercise program involving live group classes, independent home workouts, and aerobic exercise. Prescriptions were progressed as recommended by the 2019 Exercise Guidelines for Cancer Survivors. Participants completed a virtual fitness assessment and questionnaires at baseline (BL) and week 12 (12WK).

Results: Twenty-nine participants consented, 26 completed all follow-up testing (89.7%). Adherence was 89.9% (group classes), 82.7% (independent workouts), and 89.7% (additional aerobic exercise). No serious adverse events (grade ≥ 3) occurred in the study. Minor adverse events related to the intervention included grade 1 back pain (n=2), grade 2 back pain (n=1), and grade 2/3 back pain (n=1). One compression fracture unrelated to the intervention occurred during the study. Significant improvements were found for quality of life (FACT-MM) [BL: 111±23 vs 12WK: 118±19, p=0.0332], thirty-second sit-to-stand score [BL: 13.1±4.5 repetitions vs 12WK: 15.8±4.3 repetitions, p<0.0001], plank hold duration [BL: 78.3±46.0 seconds vs 12WK: 119.9±73.4 seconds, p=0.0002] and timed single leg stance [BL: 23.1±13.3 seconds vs 12WK: 31.8±12.6 seconds, p=0.0002].

Conclusion: The exercise program was feasible but associated with a higher than expected rate of musculoskeletal events. Supervision, active support, and appropriate personnel appear to be key components in facilitating feasibility. The promising findings from this study warrant further investigation with a large scale randomized controlled trial.

Keywords: Myeloma, Plasma Cell Dyscrasia, Exercise, Physical Activity, Tailored, Home

3.2 INTRODUCTION

Multiple myeloma (MM) is a plasma cell cancer that accounts for roughly 1% of cancer diagnoses and 13% of hematologic cancers (5). With a 5-year survival of ~45% and a 10-year survival of ~30%, MM has a low survival rate relative to the cancer population as a whole (5). MM is a cancer that causes osteolytic bone destruction (6), leading to deformities, pain, reduced mobility and functioning, fatigue, and increased fracture risk (7). Fortunately, treatment advances in recent decades have increased median survival from 3 to 6 years, meaning patients are living longer (10). However, patients are living with late and long-term side-effects from their treatment, including fatigue, myopathy, neuropathy, and pain (11). Care strategies are needed to improve patient function in the face of this lasting symptom burden (12).

Exercise can improve the lived experience of people living with cancer (13). Evidence compiled in the recently updated American College of Sports Medicine guidelines shows that exercise improves common cancer-related health outcomes including fatigue, anxiety, depression, physical functioning, and health-related quality of life (13). Unfortunately, these guidelines are primarily based on studies in common cancers, like breast and prostate. These consensus statements on the benefits of exercise may not apply to MM, given the unique disease- and treatment-related impairments this population experiences, including fracture risk, myopathy, and pain. In this group specifically, there is a paucity of exercise trials (14) with some studies showing promise in outcomes including strength, fatigue, and aerobic capacity (15-17), and others reporting non-significant effects from exercise (18-22). Overall, more research is required to determine what levels and kinds of exercise are appropriate for people with MM.

It has been proposed that program tailoring and supervision are key program characteristics in ensuring the success of exercise programming for people with MM (74). People with MM have also identified program flexibility as an important consideration for exercise program design (73). Home exercise programs offer flexibility, but often lack needed supervision and support (74). On the other hand, supervised programming offered at hospitals or fitness centres can be logistically challenging for patients, leading to adherence and completion issues (74). eHealth has the potential to improve care by leveraging the benefits of in-person programming (direct supervision and on-going program tailoring) with the benefits of home-based programming (flexibility and convenience).

The purpose of this study was to determine the safety and feasibility, as well as the preliminary efficacy, of a 12-week virtually supported home-based aerobic and resistance exercise program. The program aimed to support and progress the physical activity of people with MM as recommended in the 2019 Exercise Guidelines for Cancer Survivors. We hypothesized that the 12-week virtually supported home exercise program would prove safe and feasible for people with MM and would demonstrate preliminary efficacy with significant improvements in physical function and quality of life.

3.3 METHODS

3.3.1 Study Design

The Myeloma Progressive Resistance and Aerobic Exercise Study (MY PROGRESS) was a single group pre-post feasibility study. Ethics approval was received from the Health Research Ethics Board of Alberta: Cancer Committee on August 26th, 2020 (HREBA.CC-20-0201). The study was registered at www.clinicaltrials.gov (NCT04484714). Informed written consent was obtained from each participant prior to enrollment.

3.3.2 Participants

The study employed convenience sampling. A single group of participants meeting the following criteria were recruited: ≥18 years old; multiple myeloma diagnosis; in one of three treatment categories: (i) transplant ineligible, in first line treatment, (ii) transplant eligible, sufficiently recovered from transplantation (>3 months post-transplantation), (iii) relapsed/recurrent/refractory myeloma with 1+ prior lines of treatment; and able to provide informed written consent in English. Potential participants were screened using general and cancer-specific Physical Activity Readiness Questionnaires (PAR-Q+) to determine appropriateness for the exercise program. Physician approval for exercise was required prior to enrollment in the study. Exclusion criteria included physician-determined inability to exercise safely at home. Participants with AL amyloidosis, solitary plasmacytoma, or Waldenstrom macroglobulinemia, in the absence of multiple myeloma, were excluded. Participants deemed too frail to partake in a home program based on red flags from the assessment (e.g., cannot perform 1 sit-to-stand or cannot balance for > 3 seconds on one foot) were excluded and referred to the Rehabilitation Medicine Department at the Cross Cancer Institute for treatment.

Recruitment occurred through three methods: (i) eligible participants were approached by their healthcare team at outpatient appointments at the local cancer centre, (ii) through patient information presentations and study pamphlets in partnership with the local myeloma patient support society, and (iii) eligible former participants of the Alberta Cancer Exercise (ACE) program (76) that had indicated interest in future studies. To determine feasibility and inform a future larger scale effectiveness study, the target sample size was set to 25 participants, an appropriate sample size for feasibility studies of this nature (77).

3.3.3 Procedures

Participants received a 12-week aerobic and resistance exercise training program tailored to their abilities based on the 2019 Exercise Guidelines for Cancer Survivors (13). The goal was to have participants meeting current guideline recommendations of moderate intensity resistance training ≥ 2x/week and ≥ 90 minutes/week of moderate intensity aerobic exercise by study completion. Exercise programming was delivered by a Kinesiologist with >3 years of experience working in exercise oncology with oversight provided by an exercise physiologist and physical therapist.

The program was delivered through an e-Health technology titled Healthy Eating, Active Living, and Mindful Energy (HEAL-Me) (78). HEAL-Me is a web-based non-commercial application developed by a University of Alberta based research team being led by a MY PROGRESS study investigator (PT). HEAL-Me allows for the delivery of flexible, tailored home exercise programming and for this study involved three modes of delivery: (i) virtual live group exercise classes; (ii) independent, personalized home workouts; (iii) independent aerobic exercise prescription.

Resistance exercise: resistance exercise used a combination of virtual live group exercise classes and independent, personalized home workouts. Workouts/classes lasted 60 minutes and involved the following: 10 minute aerobic-based warm-up, 2 rounds of an 8-exercise circuit involving 60 seconds work and 30 seconds rest for each exercise and finished with 5 minutes of light stretching. In addition, each workout alternated between having (1) a core exercise sequence: two sets of two additional core exercises, (2) an 8-minute additional balance sequence, or (3) additional stretching between the conclusion of the circuit and the final stretches. Circuits

involved 2 cardio, 2 upper body, 2 lower body, 1 balance, and 1 core exercise. Muscle groups that are specifically impacted by MM were preferentially worked over others, including proximal limb muscle groups (4, 79), the muscles of the core, and the back. Independent workouts were assembled from a bank of exercises on the HEAL-Me app. At program start, participants were matched to one of four program start-points based on their fitness. From there, participants followed the program's pre-set myeloma-specific routine progression, with a slightly new routine prescribed each week. Adaptations were made to tailor each week's routine to the participants abilities. Group classes offered 2-3 levels of difficulty per exercise, and participants were matched to the option that was most appropriate for them. Participants progressed in exercise frequency and intensity over the 12-week program (Table 1).

Table 1. Overview of the resistance exercise prescription employed in the home program.

	Live Group Workout		Independent Workout	
Week	Frequency (sessions/week)	Target RPE (0-10)	Frequency (sessions/week)	Target RPE (0-10)
1	1	3	1	3
2	1	3	1	3
3	1	3	1	3
4	1	4	1	4
5	1	4	1	4
6	1	4	1	4
7	1	4	2	4
8	1	4	2	4
9	1	4	2	4
10	1	5	2	5
11	1	5	2	5
12	1	5	2	5

Aerobic exercise: participants were also prescribed additional aerobic exercise to meet current guideline recommendations. Participants selected the aerobic exercise they preferred (e.g. walking, elliptical, cycling). Participants baseline aerobic activity informed the aerobic exercise prescription. Participants already completing 90 minutes of moderate intensity aerobic activity were instructed to maintain that activity or were gradually progressed up to 150 minutes of moderate intensity aerobic activity, if interested. Participants who were exercising below aerobic exercise recommendations were gradually progressed up to 90 minutes of moderate intensity aerobic exercise per week based on ACSM progression principles (80). Participants monitored

their intensity using the talk test and recorded their aerobic exercise using the app's activity tracking portal.

Adherence to program prescriptions were tracked using the HEAL-Me app tracking software. Reasons for missed sessions were recorded and are reported below. Adaptations to individual programs and the reasoning behind each modification were also recorded and are reported below. Lastly, program support was provided through the messaging feature of the app, which allowed participants and exercise trainers to connect to discuss questions, concerns, and adaptations. Additionally, the research team conducted virtual one-on-one sessions grounded in motivational interviewing techniques on a regular basis (at study weeks 1, 2, 3, 5, 7, 9, 11) to discuss program design, adaptations, technique, and explore both challenges and successes that participants were experiencing.

3.3.4 Outcome Measures

The primary outcome of this study was the protocol's feasibility. Feasibility was assessed by the rate of uptake, completion rate, safety, and adherence. A feasible rate of uptake was set at ≥ 21 participants consenting to the study over a 7-month recruitment period. A completion rate indicating feasibility was set at ≥ 80% of consenting participants completing the 12-week assessment. To determine safety, adverse events were tracked and reported as per the Common Terminology Criteria for Adverse Events (CTCAE) guidelines. Due to the high risk nature of this group, the researchers monitored the participant's exercise response closely with the aim to identify potential exercises or program components that could increase the participants' symptoms, and risk of fracture or other adverse events. Safety associated with feasibility of the supported home-based program was defined as the absence of serious adverse events (≥ grade 3) related to the intervention. Adherence indicating feasibility was defined as completion of ≥ 75% of the exercise prescription.

Additional outcome measures were collected to support the effectiveness of programming and inform a future larger scale study. Surveys and physical assessments were completed pre- and post-intervention (12 weeks). Physical assessments were completed virtually. An independent assessor completed the post-intervention assessment. Physical assessments were used to determine aerobic exercise capacity, lower body muscle strength, core endurance,

balance, and both upper and lower body flexibility. Aerobic exercise capacity was assessed using the practical, simple, and low-impact two-minute step test (81). Lower body muscle strength was measured using the 30-second sit-to-stand test (82). Core endurance was measured using a plank endurance test, where participants held a plank on their forearms and toes for as long as they could. Balance was assessed using the timed one-legged stance (83). Shoulder flexibility was determined by measuring the participant's active shoulder flexion range of motion using a goniometer (84). Lower body flexibility was assessed using the modified sit-and-reach test (85). Additionally, height and weight were abstracted from medical records. In cases of significant bone involvement and/or pain, some of the above tests were not completed at the choice of the participant and/or the discretion of the research team. Reasons for non-completion were recorded and are reported.

Surveys were used to assess quality of life, fatigue, and symptom burden. Health-related quality of life (HRQOL) was measured using a series of established questionnaires and subscales from the Functional Assessment of Chronic Illness Therapy (FACIT) System. Specifically, the FACT-MM was administered (86), along with the following subscales to gather additional symptom-specific information: FACIT-Fatigue (87, 88), FACT/GOG-NTX4 (89) for neuropathy, and FACT-Bone Pain (90). Symptom burden was assessed using the Edmonton Symptom Assessment Scale (ESAS) (91, 92).

3.3.5 Statistical Analysis

Demographics, medical information, and feasibility measures are presented using descriptive statistics (mean ± SD or median (range) for continuous variables, frequency (percentage) for nominal variables). The normality of all secondary effectiveness outcomes (physical assessments and patient-reported outcomes) was tested using the Skewness-Kurtosis Test in Stata/MP. For data with non-normal distributions, pre-vs post-intervention changes were analyzed using a Wilcoxon Signed Rank Test and reported by median (range). For data with normal distributions, pre-vs post-intervention changes were analyzed using the Paired t-test. All analyses were conducted using Stata/MP (version 13.0, StataCorp LLC, College Station, TX), with alpha set to 0.05.

3.4 RESULTS

3.4.1 Participants

Recruitment began in September 2020 and continued to March 2021. Twenty-nine participants consented to the study. Twenty-eight participants completed baseline testing and began the 12-week program. The mean age of participants was 65 ± 8.4 years (sex: 14 males, 14 females). Further demographic and medical characteristics of the participants are provided in Table 2. Participants were recruited by oncologist referral (n=5), cancer centre rehabilitation staff referral (n=1), local myeloma support society (n=9), former ACE participant (n=3), and the Myeloma Canada website (n=2).

Table 2. Participant characteristics and demographics.

Variable	Mean ± SD / Median (Range)
Age (years)	65.0 ± 8.4
BMI (kg/m^2)	26.5 ± 4.9
Time Since Diagnosis (months)	35 (9-164)
# Of Lines of Treatment at Program Start	2 (1-5)
Sex	Frequency (%)
Male	14 (50%)
Female	14 (50%)
Marital Status	Frequency (%)
Never Married	2 (7%)
Married	24 (86%)
Divorced	2 (7%)
Education	Frequency (%)
Completed High School	6 (21%)
Some University/College	4 (14%)
Completed University/College	15 (54%)
Some Graduate School	1 (4%)
Completed Graduate School	2 (7%)
Family Income	Frequency (%)
Did Not Disclose	6 (21%)
$20,000-59,999	6 (21%)
$60,000-99,999	9 (32%)
>$100,000	7 (25%)
Current Employment Status	Frequency (%)
Disability	8 (29%)
Retired	15 (54%)
Part-Time	1 (4%)
Full-Time	3 (11%)
Home Maker	1 (4%)
Ethnic Origin	Frequency (%)
Caucasian (White)	26 (93%)
Southern Asian	1 (4%)
Unknown (Adopted)	1 (4%)

Smoking Status	Frequency (%)
Never Smoked	9 (32%)
Ex-Smoker	17 (61%)
Regular Smoker	2 (7%)
Drinking Status	Frequency (%)
Never Drank	1 (4%)
Ex-Drinker	3 (11%)
Occasional or Social Drinker	16 (57%)
Social Drinker	7 (25%)
Regular Drinker	1 (4%)
Current Treatment	Frequency (%)
Lenalidomide	6 (21%)
Lenalidomide + Dexamethasone	3 (11%)
Lenalidomide + Daratumumab	3 (11%)
Lenalidomide + Ixazomib	3 (11%)
Lenalidomide + Daratumumab + Dexamethasone	2 (7%)
Lenalidomide + Ixazomib + Dexamethasone	1 (4%)
Carfilzomib + Dexamethasone	2 (7%)
Carfilzomib + Cyclophosphamide + Dexamethasone	1 (4%)
Ixazomib	1 (4%)
Bortezomib	1 (4%)
Bortezomib + CC92480 + Dexamethasone	1 (4%)
Pomalidomide + Cyclophosphamide + Dexamethasone	1 (4%)
Pomalidomide + Dexamethasone	1 (4%)
Pomalidomide + Daratumumab + Dexamethasone	1 (4%)
Surveillance	1 (4%)
SCT Information	Frequency (%)
One Previous SCT	19 (68%)
>1 Previous SCT	2 (7%)
SCT in Current Line of Treatment	11 (39%)
SCT in Previous Line of Treatment	10 (36%)
Other Disease Information	Frequency (%)
Bone Disease	23 (82%)
Previous Radiation Therapy	13 (46%)
Previous Surgery[2]	8 (29%)

[1] SCT: Stem Cell Transplantation; [2] Includes vertebroplasty, kyphoplasty, or orthopedic surgeries related to myeloma

3.4.2 Primary Feasibility Outcomes

Recruitment occurred over a 7-month period, yielding a recruitment rate of 4.1 participants/month. Twenty-six participants completed the 12-week program and follow-up fitness testing (89.7%), and 27 participants completed the follow-up surveys (93.1%). Reasons for non-completion included bone pain requiring investigation and intervention prior to entering the program (n=1), and myeloma-related death (n=1). One participant completed the follow-up questionnaires but not the fitness assessment due to a spinal fracture unrelated to the exercise program (n=1). Six participants were unable to complete the sit-and-reach test (no family

member at home to assist with test [n=5], apprehension to spinal flexion [n=1]) and 6 participants were unable to complete the plank test (history of spinal injury or back pain [n=5], and inability to get onto floor [n=1]).

Adverse events both related to the intervention (n=4) and unrelated to the intervention (n=3) were identified. Two cases of mild back pain (grade 1) occurred, one during a seated version of bridging (pain in lumbar region) and the other with performing a modified low impact jumping jack exercise (pain in thoracic region). Both cases resolved within a few days and did not impact the participants' ability to complete future exercise sessions. One case of moderate back pain (grade 2) occurred following a bridging exercise. The participant paused exercise for 6 days before resuming. Finally, one case of moderate-to-severe (grade 2/3) back pain occurred following a hip flexor stretch. The participant paused exercise for 7 days, and resumed exercise after following up with, and approval from their oncologist.

One case of moderate-to-severe spinal fracture (grade 2/3) occurred, unrelated to the exercise intervention during the 11th week of the participant's program. In this case, the participant had a fall in the bathroom. The participant discontinued exercise for the remainder of the program and was unable to complete 12-week fitness testing but did complete the 12-week questionnaires. One case of moderate back pain (grade 2), unrelated to the intervention occurred when a participant slipped on ice outdoors. The participant paused exercise participation for 4 days before resuming. Finally, one case of grade 2 arrhythmia, unrelated to the exercise intervention, occurred in a participant with a history of previous cardiac intervention. The participant paused exercise participation for 10 days while the symptoms were investigated. The participant resumed programming when cleared by their cardiologist.

On average, participants completed 82.9% of the independent home workouts (18 workouts total) and 89.9% of the live group classes (12 classes total). In terms of aerobic exercise, 16 participants progressed from 40 minutes/week to 90 minutes/week, 5 participants maintained 90 minutes/week for 12 weeks, 3 participants progressed from 90 minutes/week to 150 minutes/week, and 4 participants maintained 150 minutes/week for 12 weeks. Across all participants, 89.7% of the volume of self-directed aerobic exercise prescribed in the program was completed. The most common reasons for missed workouts or aerobic exercise included: fatigue (n=20), comorbid medical issue (n=20), competing priorities (n=15), appointments/schedule

(n=12), and injury (n=11). See Figure 1 for all reasons. Exercise adaptations were necessary throughout the program to tailor the program's template routines to the needs of each individual. The most common exercise adaptations included: exercise alternatives (n=33), intensity adaptation – decreased level of difficulty (n=28), and custom routine (n=24). See Figure 2 for more information about the exercise adaptations that were made. Exercise adaptations were most commonly made due to disease-related pain (n=27), limited range of motion (n=19), high strength (n=13), history of fracture/lytic lesion in area (n=10), and non-myeloma pain (n=10). See Figure 3 for all the reported reasons for exercise adaptations.

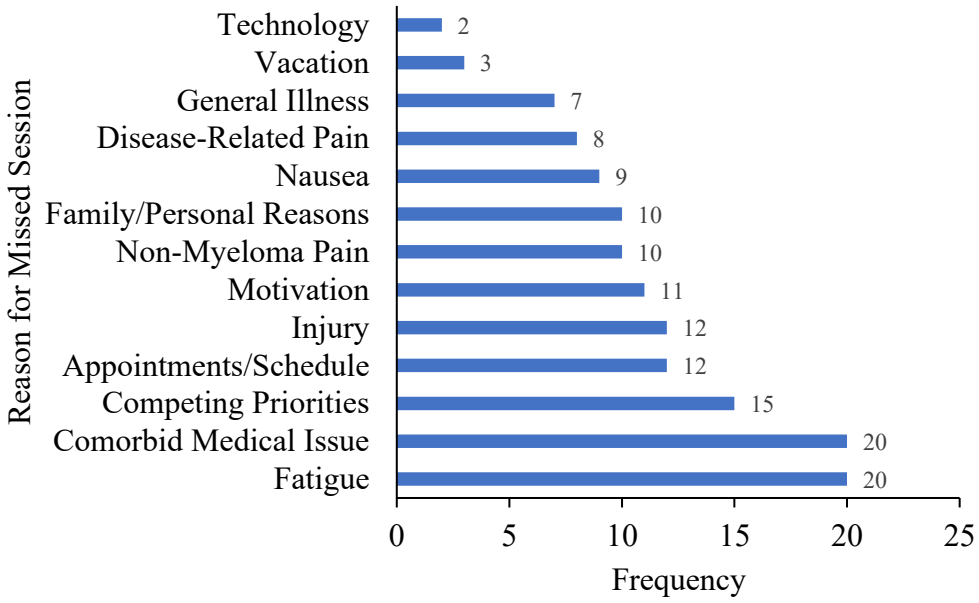

Figure 1. Participant-reported reasons for non-completion of exercise sessions (group workout, independent workout, independent aerobic exercise) during the 12-week exercise program by frequency of occurrence.

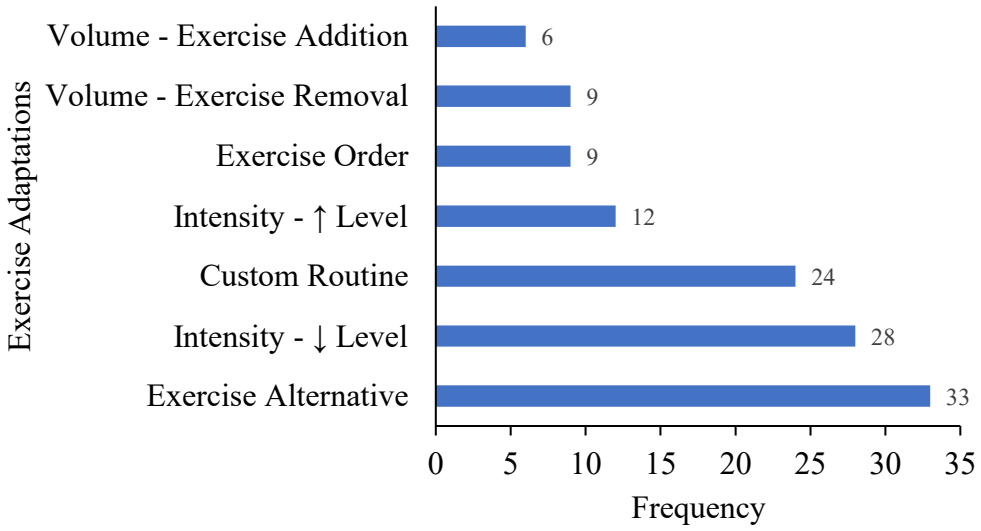

Figure 2. Exercise adaptations made for participants during the 12-week exercise program by frequency of occurrence. Exercise alternative: replacement of one exercise with another one of similar difficulty and goal. Intensity - ↓ level: an exercise of lower intensity, targeting similar muscle groups. Custom routine: all exercises were changed from the original template routine. Intensity - ↑ level: an exercise of higher intensity than the original, targeting similar muscle groups. Exercise order: the order of the exercises in the routine were adjusted to make it easier for the participant to transition between exercises. Volume – exercise removal: one or more exercises were removed and not replaced. Volume – exercise addition: one or more exercises were added without removing an exercise.

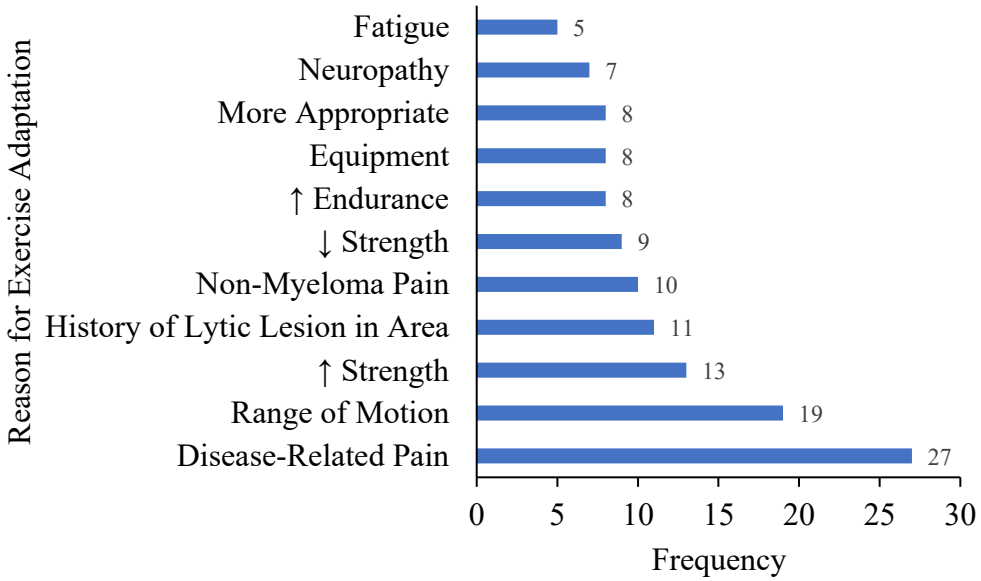

Figure 3. Reason for individual exercise adaptations made during the 12-week exercise program by frequency of occurrence.

3.4.3 Satisfaction Survey

There was a high level of program satisfaction (Table 3). The majority of participants either agreed or strongly agreed that the exercise program was beneficial (96.3%, n=26) and enjoyable (92.6%, n=25). Participants also generally either agreed or strongly agreed that the program helped them meet their health and wellness goals (92.6%, n=25) and increase their knowledge related to the benefits of exercise in multiple myeloma (88.9%, n=24). All participants either agreed or strongly agreed that they would recommend the program to other people with multiple myeloma (100%, n=27). The majority of participants felt that the service provided by the program staff was excellent (92.6%, n=25). Finally, participants were satisfied with the HEAL-Me application, with most participants either disagreeing or strongly disagreeing that it was a burden to learn how to use the app (81.5%, n=22) and to use it to complete their exercise program (88.9%, n=24).

Table 3. Participant satisfaction with the exercise program, program staff, and mobile application based on a program satisfaction survey completed following the 12-week exercise program.

	Strongly Disagree n (%)	Disagree n (%)	Neutral n (%)	Agree n (%)	Strongly Agree n (%)
Exercise Program					
The program was beneficial to me.	0 (0)	0 (0)	1 (3.7)	12 (44.4)	14 (51.9)
The program was enjoyable to me.	0 (0)	0 (0)	2 (7.4)	11 (40.7)	14 (51.9)
Completing the program helped me meet my health and wellness goals.	0 (0)	0 (0)	2 (7.4)	13 (48.1)	12 (44.4)
The program helped increase my knowledge related to the benefits of exercise for multiple myeloma	0 (0)	2 (7.4)	1 (3.7)	11 (40.7)	13 (48.1)
The program helped me manage symptoms and side effects related to my cancer and/or treatments	0 (0)	1 (3.7)	13 (48.1)	6 (22.2)	7 (25.9)
I would recommend the exercise program to others	0 (0)	0 (0)	0 (0)	4 (14.8)	23 (85.2)
Program Staff					
The program staff made me feel comfortable	0 (0)	0 (0)	0 (0)	4 (14.8)	23 (85.2)
The program staff were knowledgeable	0 (0)	0 (0)	0 (0)	2 (7.4)	25 (92.6)

The program staff were supportive	0 (0)	0 (0)	0 (0)	3 (11.1)	24 (88.9)
The program staff worked with me to ensure the exercises were appropriate for my level of fitness and my symptoms	0 (0)	0 (0)	0 (0)	4 (14.8)	23 (85.2)
Overall, the service you received from the program staff was excellent	0 (0)	0 (0)	0 (0)	2 (7.4)	25 (92.6)
Mobile Application					
It was a burden learning how to use the HEAL-Me App	17 (63)	5 (18.5)	5 (18.5)	0 (0)	0 (0)
It was a burden using the HEAL-Me App to exercise	19 (70.4)	5 (18.5)	3 (11.1)	0 (0)	0 (0)

3.4.4 Secondary Outcomes

Aerobic exercise capacity, measured by 2-minute step test scores, significantly improved from baseline (68.6 ± 17.7 steps) to 12-weeks (81.3 ± 16.0 steps, delta: 12.7 ± 10.0 steps, $p<0.0001$). Lower body muscle strength, measured by 30-second sit-to-stand score, significantly improved from baseline (13.1 ± 4.5 repetitions) to 12-weeks (15.8 ± 4.3 repetitions, delta: 2.7 ± 2.7 repetitions, $p<0.0001$). Core endurance, measured by plank duration, significantly improved from baseline (78.3 ± 46.0 seconds) to 12-weeks (119.9 ± 73.4 seconds, delta: 41.6 ± 42.3 seconds, $p=0.0002$). Balance, measured by the timed single leg stance test, significantly improved from baseline (23.1 ± 13.3 seconds) to 12-weeks (31.8 ± 12.6 seconds, delta: 8.7 ± 10.1 seconds, $p=0.0002$). Upper body flexibility, measured by the bilateral average of active shoulder flexion range of motion, significantly improved from baseline (146.8 ± 11.7 degrees) to 12-weeks (149.4 ± 11.5 degrees, delta: 2.6 ± 4.7 degrees, $p=0.0084$). Finally, lower body flexibility, measured by the bilateral average of the modified sit-and-reach distance, significantly improved from baseline (-5.8 ± 14.0 cm) to 12-weeks (-2.2 ± 13.6 cm, delta: 3.6 ± 4.5 cm, $p=0.0014$).

Health-related quality of life, measured by the 41-item FACT-MM, significantly increased (improved) from baseline (111 ± 23) to 12-weeks (118 ± 19, delta: 7 ± 17, $p=0.0332$). There was no significant change in self-reported fatigue, measured by FACIT-Fatigue Subscale, from baseline (35 ± 10) to 12-weeks (37 ± 8, delta: 2 ± 8, $p=0.2806$). There was no significant change in symptoms of peripheral neuropathy, measured by the 4-Item FACT/GOG-NTX, from

baseline (6.1 ± 3.5) to 12-weeks (6.9 ± 4.1, delta: 0.7 ± 3.3, p=0.2849). There was no significant change in bone pain, measured by the FACT-BP subscale, from baseline (median: 49, range: 19-59) to 12-weeks (median: 49 range: 28-59; delta median: 0, delta range: -17-20; p=1.0).

There was a significant decrease in physical symptom burden, measured by the ESAS physical subscore, from baseline (median: 6, range: 0-27) to 12-weeks (median: 2, range: 0-12; delta median: -4, delta range: -23-0; p<0.0001). 18 participants achieved a minimal clinically important difference (change ≥ 3 points) (93). However, there was a significant increase in psychological/emotional symptom burden, measured by the ESAS psychological subscore, from baseline (median: 2, range: 0-15) to 12-weeks (median: 8, range: 0-25; delta median: 4, delta range: -13-25; p=0.0056). There was no significant change in total symptom burden, measured by the ESAS global score, from baseline (median: 10.5, range: 0-43) to 12-weeks (median: 12, range: 0-35; delta median: 1, delta range: -31-21, p=0.8193).

3.5 DISCUSSION

Findings from this study indicate that: (1) the program was feasible but associated with a relatively high rate of musculoskeletal events, (2) participants were satisfied with the program, program staff, and mobile application, and (3) participants experienced significant improvements in physical function and quality of life over the course of the program.

3.5.1 Safety, Feasibility, and Satisfaction

All feasibility targets set for this study were met. The low attrition rate (10.3%) in this study compares favourably to previous studies with attrition rates of 15-42% (16, 18, 21, 66). Further, adherence to the exercise program was high, with participants completing 89.9% of the group workouts, 82.9% of the independent home workouts, and 89.7% of the prescribed aerobic exercise. Taken together, these results support the acceptability of the exercise program for people with MM. Although our results indicate that a virtually-supported home exercise that progresses towards the 2019 ACSM Exercise Guidelines for Cancer Survivors (13) is feasible in MM, the program included components above and beyond what might typically be included in home programming. Specifically, two key features may have contributed to the acceptability of the exercise program: (1) the tailored nature of the program, and (2) the inclusion of supervision

and active support. This study is the first to systematically document how programming was tailored to people with MM. Despite the program being myeloma-specific, individual participants required further adaptations on a weekly basis to ensure programming was appropriate for them. This varied from small adjustments like finding alternative exercises of similar difficulty to developing an entirely new custom routine for the participant. Importantly, myeloma-related pain and history of fracture/lytic lesion in area were two of the primary reasons why programming needed further adaptations for specific participants. These symptoms represent significant barriers to people with MM (70, 71). In the absence of purposeful program changes that accommodate for these symptoms, the program may not be tolerated by participants.

In addition to tailoring, supervision has been proposed to enhance effectiveness and appropriateness of programming for people with MM (74). Indeed, it appears that exercise programs that are supervised are more effective that unsupervised programs for people living with cancer (13). In the current study, this involved weekly supervised workouts in a one-on-one or small group setting and regular check-ins between the participant and the exercise specialist. These features allowed the exercise specialist to provide specific feedback to participants about their form and facilitated discussion on how the program was going, which informed exercise adaptations and tailored education/advice from the specialist.

Beyond tailoring and active support, skilled and experienced exercise personnel are likely needed to deliver a safe and effective exercise program for people with MM. In this study, a kinesiologist with > 3 years of experience working with this population delivered the exercise program. The kinesiologist was supported by a team including a physiotherapist with > 20 years of experience in cancer rehabilitation, a cancer-specific clinical exercise physiologist, and a hematologist/oncologist to ensure programming was appropriate for all participants. This is in line with the National Comprehensive Cancer Network (NCCN) Survivorship Guidelines (94), which recommend medical evaluation/clearance by a medical professional for patients with poor bone health and inclusion of physiotherapists, exercise physiologists, or equivalent in exercise program development. Participants felt this delivery model was excellent, indicating that staff were knowledgeable, supportive, and comforting, and worked with them to ensure the exercises fit their needs and abilities. We recommend that future studies in MM also carefully consider the

personnel delivering the exercise program and ensure sufficient safety checks are in place to keep participants safe.

No serious adverse events (≥ grade 3) related to the intervention occurred during the study. Despite tailoring, active support, and skilled and experienced personnel; however, there was a higher than usual rate of musculoskeletal events reported in this study when compared to other tumour types or conditions. Interestingly, many previous studies in MM failed to report on adverse events (18, 20, 62) or reported that no adverse events related to the intervention occurred (15, 16, 19, 21). Further, several studies excluded participants with bony disease (15, 16, 21, 68), those who are likely at higher risk of events. A recent meta-analysis found that exercise increases participants' risk of non-serious adverse events but does not increase risk of serious adverse events (95).This meta-analysis included participants both with or without medical conditions but excluded participants receiving chemotherapy, so it remains unclear how exercise might modify the risk of adverse events in MM. It is likely not possible to completely eliminate the potential for an increased risk of adverse events in a sufficiently dosed exercise program in this population. Researchers should thus anticipate a greater rate of adverse events, as well as challenges in prescribing exercise to participants. Alongside these risks, there is still potential for people with MM to significant benefit from exercise programming (96). Program delivery personnel and participants must be aware of the potential risks and benefits of exercise and decide what level of activity is appropriate based on the participant's condition. Additionally, researchers should aim to minimize the likelihood and severity of events by ensuring programming is individually tailored, assisted by active support, and delivered by appropriate qualified personnel.

3.5.2 Effectiveness

Participants experienced promising changes over the course of the 12-week program, which warrant further investigation in a randomized controlled trial. Significant improvements in leg strength were observed in the current study, supporting the findings of Groeneveldt et al. (16). Improvements in leg strength may be of particular importance in this population, given the negative impacts of prolonged corticosteroid use on proximal muscle strength (4, 79). Lower extremity muscle weakness may increase fall risk (97), and therefore, fracture risk (98) within the MM population. Indeed, people with MM have an elevated fall risk (99). Given the

association between skeletal events and morbidity, mortality, and hospital costs (100, 101), reducing fall risk by strengthening the muscles of the leg and hips is recommended for future exercise programming for MM. In conjunction with leg strengthening activities, it may also be beneficial to include balance exercises, as a specific training component to improve balance.

Participants also experienced improvements in core strength/endurance in this study. To our knowledge, core strength has not been included as an outcome in previous exercise trials in MM. Furthermore, many of the previous trials do not explicitly state whether core exercises were included in the prescription (15, 16, 18, 20). Strength in the core, which includes the muscles in the abdominal wall, low back and pelvis, is associated with dynamic balance (102), which is a predictor of fall risk and fractures (98). Core strength may have contributed to the improvements in balance that were observed in this study. Additionally, back extensor strengthening can help improve posture, reduce axial deformity (103), which reduces chronic back pain associated with kyphosis (3) and has been shown to prevent vertebral fractures in osteoporosis (104). Taken together, the potential benefits of core exercises for improving back pain, posture, and fracture risk in MM support the inclusion of these exercises within a myeloma-specific exercise program. However, these exercises should be individually tailored to the participant with consideration given to positioning to minimize forces and loading on the spine to minimize the risk of adverse events and exacerbations of back pain as observed in this study.

Further to these changes in physical function, a significant improvement in health-related quality of life was observed in this study. The current exercise program may also help manage symptom burden, as participants experienced improvements in physical symptom burden. These are important findings, as people with MM experience a low health-related quality of life and a high symptom burden (105). However, psychological symptom burden worsened over the course of the program. This contradictory finding may be explained by the significant impact that COVID-19 has had on the incidence of anxiety and depression amongst people living with cancer (106). Despite improvements in health-related quality of life, no change in fatigue was observe in this study. Improvements in fatigue have been observed in previous single group studies in MM (16, 62), but have yet to be reproduced in a randomized control trial (21, 68). Further research on the potential impact of exercise on quality of life and symptom burden, particularly common symptoms in MM, such as pain and fatigue, is warranted.

3.5.3 Limitations

This study is not without limitations. First, this is a single group study. Without a control group, it is not possible to distinguish between the effect of the treatment, a placebo effect, and the effect of time. This design was chosen as the focus on this study was feasibility rather than efficacy, given the inconsistencies of results from previous research in MM and because it is still not clear whether virtually-delivered programming is safe in this population. The effects of this exercise program on physical function and quality of life should be confirmed using a randomized controlled trial to discern whether the changes can be attributed to the intervention itself. Secondly, gold standard measures of physical function were not used. Although gold standard assessments, such as a cardiopulmonary exercise test are the most accurate method of determining an individual's fitness, they require significant equipment and attendance from the participant at a testing facility. This creates a barrier to participation for people living with cancer in rural/remote communities. Additionally, delivery of in-person assessments has not been possible in our region for the majority of the COVID-19 pandemic. To minimize risk of transmission, remote fitness assessments have been recommended (107). Importantly, the selected assessments have established validity/reliability and were completed by trained personnel.

3.6 CONCLUSION

The 12-week virtually supported home exercise program was feasible in a sample of people with MM but was associated with a higher than expected rate of musculoskeletal events. Researcher should anticipate higher rates of adverse events in this population and ensure they are prepared to record and respond to events. Programming should be individually-tailored, and include supervision, active support, and well-trained personnel in order to manage the possibility of both serious and non-serious adverse events. It remains unclear whether the current physical activity recommendations for people living with cancer are feasible for people with MM, as participants in the current study were slowly progressed up to guideline-recommended volumes but were not monitored beyond the study period. Thus, it is unclear if they were able to maintain the dose for the recommended 8-12 weeks. Future studies could employ a longer duration intervention that both supports participants to reach recommendations and includes a follow-up monitoring period. A large scale randomized controlled trial is warranted to confirm the effects

of the current exercise program on fitness outcomes including leg strength, core strength, balance, as well as quality of life and symptom burden.

CHAPTER 4: EXPLORING PARTICIPANT PERCEPTIONS OF A VIRTUALLY-SUPPORTED HOME EXERCISE PROGRAM FOR PEOPLE WITH MULTIPLE MYELOMAL A QUALITATIVE STUDY

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4.1 ABSTRACT

Introduction: Supervision, tailoring, and flexibility have been proposed as key program elements for delivering successful exercise programs for people with Multiple Myeloma (MM). However, no studies to date have evaluated the acceptability of an intervention specifically employing these components. The aim of this study was to determine the acceptability of a virtually-supported exercise program and eHealth application in people with MM.

Methods: A qualitative description method was used. One-on-one interviews were conducted with participants who completed the exercise program. Content analysis was used to analyze verbatim transcripts from interviews.

Results: 20 participants were interviewed (64.9 ± 6.7 years of age, n=12 females). Participants had positive perceptions of the exercise program. Three themes emerged related to strengths/limitations: *One Size Does Not Fit All*, *App Usability*, and *Sustainability*. *Supportive and Responsive Programming* was a main strength of the program, characterized as programming that was tailored, involved active support, and delivered by appropriate personnel. The inclusion of *Diverse Exercise Opportunities* was also regarded as a strength, as it accommodated the preferences of all participants. Participants felt the app was simple and user friendly but had a few less intuitive components. Finally, participants wanted the study to transition into a sustainable, ongoing program.

Conclusions: The virtually-supported exercise program and eHealth application were acceptable for people with MM. Programs should employ tailoring, active support, and appropriate personnel to bolster acceptability, and include both supervised and flexible exercise formats. eHealth apps should be simple to use to ensure technology proficiency is not a barrier for participants.

4.2 INTRODUCTION

Multiple myeloma (MM) is an incurable cancer of plasma cells associated with significant morbidity (7). There are an estimated 160,000 new cases of MM and 106,000 MM deaths that occur yearly around the world (108). Although incurable, recent advances in treatment have extended median survival to 6 years (10) and 10 years in those who are eligible for autologous stem cell transplantation (37). However, treatment needs to be intensive and prolonged to achieve these survival rates. The pathophysiology of MM and its associated therapies cause an array of debilitating side effects, including deformities, pain, reduced mobility and functioning, fatigue, neuropathy, and fracture risk (7). Supportive care strategies are needed to bolster patient function in the face of this burden (12).

One emerging supportive therapy that may be of benefit for people with MM is exercise (14, 74). Exercise has demonstrated numerous physical and psychological benefits for people living with cancer (13), but there remains a paucity of research into the potential role of exercise as a supportive therapy in MM (14). The MM community have identified an interest and preference for a combination of aerobic and resistance exercise performed at a light- to moderate-intensity (73). However, the proportion of people with MM who meet physical activity guidelines is low (70-72). It has been proposed that program tailoring and supervision might be necessary to facilitate both increased participation in and benefits from exercise programming in this population (74). Indeed, people with MM have identified individualization as an important attribute in exercise programming (73). They have also identified the importance of program flexibility (73). These program characteristics are likely important because patients report that MM symptoms and treatment side effects including fatigue, pain, concern about bone fractures, back pain, foot weakness, and fear of infections are key barriers to physical activity (71). However, no studies to date have evaluated the acceptability of interventions that employ elements of supervision, tailoring, and flexibility for people with MM.

In the current study, we are interested in exploring participant perceptions of a novel tailored exercise program for people with MM that balances the benefits of supervision in centre-based programs with the benefits of flexibility in home programming. The Myeloma Progressive Resistance and Aerobic Exercise Study (MY PROGRESS) was a 12-week virtually-supported home exercise program delivered using a novel exercise eHealth app, the Healthy Eating, Active

Living, and Mindful Energy (HEAL-Me) App. The program involved a combination of supervised group exercise sessions and independent exercise sessions delivered directly through the HEAL-Me App. Exercise was tailored to the participants' abilities and limitations and focused on common fitness limitations present in MM, including endurance, core strength, balance, and proximal muscle strength. Regular one-on-one sessions grounded in motivational interview practices were conducted between the exercise specialist and participants to ensure programming was meeting participant needs. The program involved a progressive combination of aerobic and circuit-based resistance exercise aimed to progress participants up to the 2019 Exercise Guidelines for Cancer Survivors by program end (13). Further details on MY PROGRESS are found elsewhere (Chapter 3).

This study is grounded in patient-oriented research approaches, which engages patients as partners in an effort to improve healthcare services and practices (109). Specifically, this study employs a method and data generation strategy that aimed to refine the MY PROGRESS program and the HEAL-Me application to better meet the needs of people with MM. Qualitative methods - which are being used increasingly to explore the implementation of health research interventions (110) - were chosen for this study. Quantitative methods alone cannot elicit rich descriptions of patient experiences, whereas qualitative methods allow us to explore participant perceptions of the exercise program and app. The purpose of this study was to determine the acceptability of a virtually-supported home exercise program, defined by: (i) participants' perceptions of the virtually-supported home exercise program and application, and (ii) participants' perceptions of the strengths and limitations of the exercise program and application. Overall, we were interested in understanding participant perceptions of the MY PROGRESS program and the HEAL-Me application in order to inform both future exercise program design and a newly refined version of the HEAL-Me App.

4.3 METHODS

4.3.1 Study Design & Setting

The present study is a part of a larger multi-method feasibility study of the Myeloma Progressive Resistance and Aerobic Exercise Study (MY PROGRESS) (111). This qualitative

study was designed to complement the quantitative feasibility measures by eliciting participant feedback to develop a deeper understanding of program acceptability. Ethics approval was received from the Health Research Ethics Board of Alberta: Cancer Committee on August 26th, 2020 (HREBA.CC-20-0201). The study was registered at www.clinicaltrials.gov (NCT04484714).

This study was coordinated by the lead author, a kinesiologist and graduate student with >3 years of exercise oncology experience. The lead author was supported by a team of researchers and clinicians with expertise in the areas of cancer rehabilitation (CE, MA, MM), qualitative methods (FS, CE, MA), implementation science (MM, PT) and hematologic medicine (CV). Reporting in this article follows the published Standards for Reporting Qualitative Research (SRQR) (112).

4.3.2 Procedures

A qualitative description method was used (113). Qualitative description is used to develop an understanding of a phenomenon of interest (i.e., the experience of exercising at home using the HEAL-Me App). The resulting product is not highly abstracted and provides a description of participant experiences and feedback (114). This method allowed the researchers to explore participant experiences in order to determine the acceptability of the exercise program and eHealth application.

Purposive sampling was used to recruit for this study. Participants who completed MY PROGRESS were recruited until saturation was reached (115). Participants were contacted by phone after completing the 12-week exercise program and asked to participate in the semi-structured interview. If interested, an information letter and consent form was sent by email, and written informed consent was obtained prior to the interview. By approaching all participants in MY PROGRESS to complete this study, we aimed to gather diverse and representative perspectives. The final sample size of 20 aligns with previous qualitative research investigating exercise in people with MM (71, 73).

One-on-one semi-structured exit interviews were conducted through videoconferencing software familiar to participants (Zoom). The goal of the interview was to understand participant experiences and gather insight into how the program and application could be improved. The

interview guide was developed by the research team based on the research objectives. The interview guide was structured in three main parts: the participant's overall impressions, their perceptions of the strengths and limitations of the program and app, and suggestions for improvement.

4.3.3 Analysis

Transcripts were audio recorded and transcribed using the Zoom automated transcription software. All transcripts were reviewed for accuracy and corrected prior to analysis. Next, transcripts were uploaded to Atlas.ti, a data organization software. Content analysis was used to analyze the data as it aligns with qualitative description (113). An a priori codebook was developed based on the three main parts of the interview guide and a preliminary analysis of the data. Coding was conducted by a team of four researchers (GP, FS, MAO, CE) in three stages. At each stage, coders were paired up and independently read and coded 3-4 transcripts (116). Briefly, this process involved applying codes to segments of data that corresponded to the research objective. Segments of data describing the same idea were coded the same. Each transcript was read multiple times to ensure accuracy throughout the coding process. After coding was complete, the two independent coders met and resolved discrepancies in coding through consensus. Prior to advancing to the next stage, the team of four met to discuss data analysis and ensure codes were being assigned consistently across coders. Additionally, the codebook was revised and expanded to reflect emerging codes at each meeting. This process was then repeated until all transcripts were completed. Once all transcripts were coded, the lead author combined codes into categories, and if possible, combined categories into themes. The research team then met to discuss and refine the themes and categories. Illustrative quotes were selected to support study findings. Quotes have been cleaned to remove duplicated words and words such as "um, ah, like, and yeah" to improve readability, based on recommendations from Standing (117).

4.3.4 Rigour

Rigour is important for ensuring that the findings are accurate representations of participants' experience (114). It involves attending to research design, data collection, data analysis, and reporting (114). The criteria outlined by Guba and Lincoln (1982) were followed to

ensure methodological rigour (118). As it relates to confirmability, the research team generated and maintained a clear audit trail and all study data and documents were retained. As it relates to dependability, first, interview questions were developed based on the research objective(s). Second, the questions were trialed through a practice interview. Third, a preliminary codebook was developed a priori based on the interview guide and preliminary analysis. Fourth, one researcher completed all interviews. Fifth, data collection and analysis occurred simultaneously. Strategies to ensure credibility (internal validity) included using multiple independent coders (116) , regular peer debriefing between coders, providing verbatim quotes from participants in text for readers, and prolonged engagement (the interviewer supported the interviewees through their 12-week exercise program, taught them how to use the application, completed their fitness appraisals, and was their point of contact for issues with the program and application). Strategies to ensure transferability included providing a detailed description of participant characteristics and identifying future directions.

4.4 RESULTS

Twenty participants were interviewed, who were 64.9 ± 6.7 years of age and predominantly female (n=12). Additional details on participant characteristics are available in Table 4. The following sections will describe participant perceptions of (1) the virtually-supported home exercise program, and (2) the strengths and limitations of the program and application. Strengths and limitations are further organized into three themes: *One Size Does Not Fit All*, *App Usability*, and *Sustainability* (Figure 4). Illustrative quotes are included throughout to highlight the participants' voice.

Table 4. Participant demographic and medical information.

Variable	Mean ± SD / Median (Range)
Age (years)	64.9 ± 6.7
BMI (kg/m^2)	26.8 ± 5.2
Time Since Diagnosis (months)	31 (9-134)
# Of Lines of Treatment at Program Start	2 (1-5)
Sex	Frequency (%)
Male	8 (40%)
Female	12 (60%)
Marital Status	Frequency (%)
Never Married	1 (5%)
Married	17 (85%)
Divorced	2 (10%)

Education	Frequency (%)
Completed High School	5 (25%)
Some University/College	4 (20%)
Completed University/College	9 (45%)
Some Graduate School	1 (5%)
Completed Graduate School	1 (5%)
Family Income	Frequency (%)
Did Not Disclose	4 (14%)
$20,000-59,999	4 (14%)
$60,000-99,999	6 (21%)
>$100,000	6 (21%)
Employment Status	Frequency (%)
Disability	7 (35%)
Retired	9 (45%)
Part-Time	1 (5%)
Full-Time	2 (10%)
Home Maker	1 (5%)
Ethnic Origin	Frequency (%)
Caucasian (White)	18 (90%)
Southern Asian	1 (5%)
Unknown (Adopted)	1 (5%)
Smoking Status	Frequency (%)
Never Smoked	6 (30%)
Ex-Smoker	14 (70%)
Regular Smoker	0 (0%)
Drinking Status	Frequency (%)
Never Drank	1 (5%)
Ex-Drinker	2 (10%)
Occasional or Social Drinker	13 (65%)
Social Drinker	4 (20%)
Current Treatment	Frequency (%)
Lenalidomide	6 (21%)
Lenalidomide + Ixazomib	3 (11%)
Lenalidomide + Dexamethasone	2 (7%)
Lenalidomide + Daratumumab	2 (7%)
Lenalidomide + Ixazomib + Dexamethasone	1 (4%)
Carfilzomib + Dexamethasone	1 (4%)
Ixazomib	1 (4%)
Bortezomib + CC92480 + Dexamethasone	1 (4%)
Pomalidomide + Cyclophosphamide + Dexamethasone	1 (4%)
Pomalidomide + Dexamethasone	1 (4%)
Pomalidomide + Daratumumab + Dexamethasone	1 (4%)
SCT Information	Frequency (%)
One Previous SCT	16 (80%)
>1 Previous SCT	1 (5%)
SCT in Current Line of Treatment	8 (40%)
SCT in Previous Line of Treatment	9 (45%)
Other Disease Information	Frequency (%)
Bone Disease	17 (85%)
Previous Radiation Therapy	10 (36%)
Previous Surgery[2]	7 (25%)

[1] SCT: Stem Cell Transplantation; [2] Includes vertebroplasty, kyphoplasty, or orthopedic surgeries related to myeloma

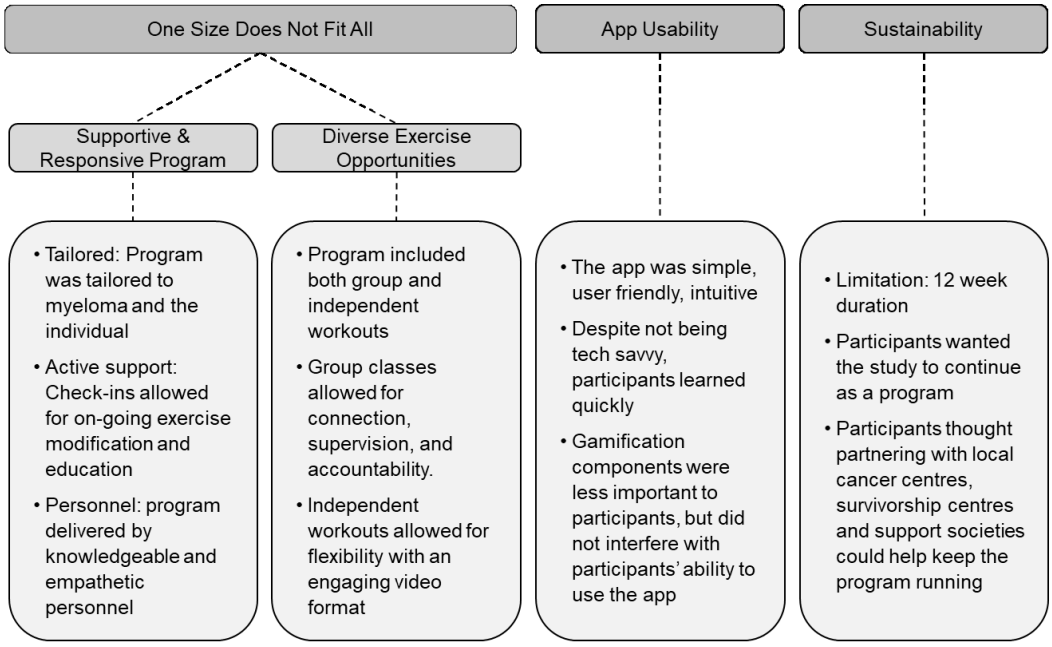

Figure 4. Emergent themes, categories, and key findings from participant interviews.

4.4.1 Participant Perceptions of the Program

Overall, participants enjoyed the exercise program and spoke favourably about their experience in the program. Participants found the program easy to access and begin. Many participants reiterated several times throughout the interview how great the program was for them or how much they enjoyed it. One participant shared: "*I cannot say how grateful I am for this program*" (P4). Indeed, some participants mentioned that they would and/or did recommend the program to other people with MM.

Participants also described how the program lessened their feelings of isolation during the COVID-19 pandemic, improved how they felt, and taught them how to perform exercise properly and safely. The latter gave participants the confidence they needed to exercise. As one participant explained: "*It gave me back my confidence that I can do more than I thought I could with this disease*" (P2). Participants explained that the program was appropriate for them, describing it as realistic, safe, and effective. One participant said "*If you give me more*

[exercise], I'll do it and then I'll hurt myself, you know? So, I think [the program] is appropriate for people with [myeloma]… I think it kept it at a spot that was safe, yet effective" (P17).

The virtual nature of the program was regarded positively by participants. Some participants thought that virtual programming was a good model regardless of the impacts of COVID-19, while other participants thought virtual delivery was specifically important during the COVID-19 pandemic. Participants shared their perspectives on the strengths and limitations of the program's virtual delivery. First, participants heavily valued that the virtual program reduced their risk of infection, given their compromised immune systems. Some participants specifically felt this way due to COVID-19, but others explained that even without COVID-19, they would be wary of going to a public gym due to the risk of infection. One participant explained: "*you don't have to worry about [equipment] being handled by people. A lot of us in our conditions are susceptible to problems with immunity, so it's very important to have a clean environment. Being at home, you've got that*" (P6). Participants also described the home as a comfortable environment for them in comparison to gym facilities. Participants in communities outside of the Edmonton Metropolitan Area appreciated the opportunity to participate in the study, which would not have been possible if it had been in-person. Finally, participants described the virtual program as convenient. It was easier for them to fit exercise into their day, and they didn't have to deal with driving and parking.

Despite the overwhelming positive feedback, participants identified limitations of a virtually delivered exercise program. Some participants felt that they couldn't interact with other participants as well through virtual means as opposed to in-person programming. In response, some participants suggested having unstructured catch-up sessions following the group exercise classes to allow for more interaction between participants. Some participants also shared that it was challenging to motivate themselves to exercise at home, often because of household distractions and not having all their exercise sessions scheduled in at specific times (i.e., the independent workouts were not scheduled). As one participant explained:

> "*I tend to think that being at home makes us a little bit lazy, though… It's not like okay, I've got to go get in the car, go to the [gym] and away you go. It's like a really scheduled event. A couple of times there I had to [join] in five or ten minutes late because I had forgotten or didn't have an alarm set. So that would be the negative side*" (P6)

4.4.2 One Size Does Not Fit All

A primary theme that emerged from the interviews was *one size does not fit all*, which includes two sub-themes: *supportive & responsive programming* and *diverse exercise opportunities*. *Supportive and Responsive Programming* was a main strength of the program and was characterized by participants as programming that was tailored to myeloma and the individual, involved active support, and was delivered by appropriately trained personnel. The inclusion of *Diverse Exercise Opportunities* (i.e., live group classes and independent home workouts) was also regarded as a strength by participants, as it accommodated for varying preferences.

Supportive and Responsive Programming

Participants valued that the program was specific to MM. One participant said: "*what was really good, at least for me, was that it addressed our issues… all the things that we as patients in multiple myeloma experience. So, it's directed to us, and it's noticeable. And I think, you know, that's really perfect*" (P10). Participants felt that having a myeloma-specific program allowed them to realize benefits specific to their disease and treatments, such as improved core strength, back strength, and balance. They also appreciated that the app was designed for people living with cancer and described it as welcoming and non-judgemental (e.g., exercises in the app are demonstrated by people living with cancer).

Participants also valued that their workouts were individually-tailored to their specific abilities and limitations. This included tailoring to their myeloma, comorbid conditions like osteoarthritis and previous orthopedic surgeries, as well as adjusting the program to fit their goals, preferences, and exercise experience. Participants enjoyed working with the exercise specialist to find alternative exercises that fit them best. Indeed, participants felt as though tailoring made exercising safer. As one participant shared: *"it's a great program built on my limitations, which is exactly what I needed... [tailoring] takes the worry, like you don't worry about the exercises you're doing because you know they're safe"* (P5).

Participants described what tailoring looked like from their perspective. Tailoring involved receiving active support from the trainer that was responsive to their needs. Specifically, the specialist-participant check-ins gave the specialist the chance to modify the

participant's program if and when issues arose and coach them on proper exercise technique. One participant shared their perspective on the check-ins: "*it was wonderful because you could see if I was doing the exercises correctly, and I could see you adapting some of the exercises… modifying the exercises so that I could do it. That was a great part*" (P15). Active support also provided a personal connection between the specialist and the participants that wouldn't otherwise be present.

Participants thought that having the right program personnel was important to engage participants and to ensure appropriate tailoring. Specifically, participants valued the exercise specialists' ability to form a therapeutic relationship, as well as their knowledge and expertise. The specialists were described as being empathetic of the participants' condition; they were seen as patient, caring, comforting, humorous, and motivational. This made participants more comfortable engaging with the program. As noted above, safety was a primary concern for participants, and it was very important to participants that the exercise specialists were knowledgeable about how to safely prescribe exercise to people with MM. Participants felt they could trust the specialist, which gave them the confidence and inspiration they needed to exercise. Many participants also felt a layer of safety was added by having their oncologist on board and involved in their exercise clearance. When asked what the most important part of the program was, one participant stated:

> "*I needed someone to tell me no, you can't do that exercise because it stresses this, you know, so whatever people are having struggles with, you need to be confident in that the person is giving you the right exercises. So I would say [the exercise specialist] is number one for sure.*" (P5)

Diverse Exercise Opportunities

A strength of the presented study was the inclusion of both live group classes as well as independent workouts. This was seen as valuable because some participants preferred the group classes, while others preferred the independent workouts. Several participants liked having access to a combination of both options. It was clear from participants that neither option was better than the other. Rather, it was important to provide both options as they complemented one another as demonstrated by the fact that many of the strengths of group classes were limitations

of the independent workouts, and vice versa. To illustrate this, a detailed description of the strengths and limitations of group classes and independent workouts is presented below.

In the group classes, participants enjoyed having other people with MM to exercise and communicate with. One participant shared that the group classes gave them "*the sense of team, you know? You see the other people working out, and you're not alone in this cancer treatment stuff here… And you know, it's a little comforting*" (P19). Participants described feeling more driven in these workouts than in the independent workouts and shared that they felt more accountable to the group classes, since they were scheduled in at specific times. Participants liked that the group classes had supervision, live feedback on form, and interaction with the specialist. This was especially valued as participants perceived this as adding a layer of safety to the program. One participant shared how their perspective changed after they injured themselves during the stretches in an independent workout: "*After that spasm and collapse, I've been much more aware of the fact of exercising alone here. So that's a small barrier [of the independent workouts], whereas in a group setting, you have someone watching or a spotter in a live session*" (P11). Participants also liked that there were multiple class times available each week, so they could attend the one that worked best for them. Finally, participants felt that the group classes were more responsive than the independent workouts. Specifically, they liked the pacing of the group classes because the timing between the exercises was adjusted based on, for example, how long participants were taking to get up and/or down from the floor. However, the group classes had limitations. First, participants explained that the explanations/demonstrations that were provided at the start of class to orient participants to the day's workout were too long, despite some finding them helpful. To address this feedback, longer videotaped explanations of the workouts (~7-8 minutes) were sent to participants prior to class, so participants could still be prepared, but the explanation during class could be more concise (~3-4 minutes). Secondly, some participants, particularly those using smaller devices like tablets, felt that it was harder to see the exercises in the group class because the screen was split in two, with two exercise options being presented at all times, instead of just one option, like in the independent workouts. One participated said: "*It was very small on my iPad. It would have been easier for me to just touch something, I'd see [one option], touch something else, I'd see [the other option]*" (P4).

For the independent workouts, participants enjoyed the follow-along continuous video format of delivery. This kept the workouts engaging. As one participant shared: "*The actual fact that it was on video and timed on video, and all of that, I think was kind of a key part to it*" (P8). The audio provided in the videos on technique, breathing, and reminders about posture and core engagement were valued by participants. Participants also felt the independent workouts offered flexibility, allowing them to complete the workouts whenever it was most convenient for them.

However, the independent workouts also had limitations. First, participants found it harder to motivate themselves to complete these workouts and felt that the lack of interaction in these workouts was a limitation. One participant said: "*I enjoy being around people and interacting with people. So the live part, where we're online together is good for me because I feel like I'm in a real class. Where the [independent workouts], I feel alone*" (P2). Participants felt there could be an increased risk of injury in these workouts, given that they were not being supervised like the group classes. Additionally, exercise adaptations couldn't happen on-the-spot, and instead, had to happen before or after. Some participants suggested having an alternative exercise presented either before or during the workout video, so if they needed an adaptation, they could select or follow the alternative exercise. Finally, some participants felt that the pacing in these workouts wasn't as good as the group classes. They found that the time/space between exercises was sometimes too short, and sometimes too long.

4.4.3 App Usability

In general, participants had positive perceptions of the app and thought it was user friendly. They described the app as simple, intuitive, and helpful. They felt it was age-appropriate and not overwhelming. One participant said "*It was so user friendly, that you know, anybody could use it. It was great*" (P12). Despite positive perceptions, participants shared they did not have much experience using technology, making it harder for them to interact with the app at the beginning. This led to a learning curve as they adjusted to using the technology. Even with this learning curve, participants were able to engage with the app exercise section quickly.

Participants identified a few aspects of the app that were less intuitive and/or contained glitches. Some participants were confused by the steps required to log their independent workouts. Participants also identified a known issue with the app where workouts did not appear

to log on the patient-facing screen, despite logging properly on the back-end. Finally, participants identified cases where the app 'acted out'. This included situations where participants pressed buttons and the app was either slow to respond or didn't seem to register their action, as well as situations where the app would stall in the middle of the independent workouts before resuming. Interestingly, participants qualified these "glitches" by reiterating their lack of technology experience. They felt these errors may be user errors, rather than app issues. As one participant said:

> "*The HEAL-Me App, partially could be me, I found a few, you know that there were glitches on occasion. And again, could be me, I found a bit of confusion… I am not on the computer doing those kinds of things all the time, so that could be part of it*" (P4).

Importantly, none of the glitches or issues with the app prevented participants from using the app and completing their exercise.

The HEAL-Me App had additional features including additional supportive information for the exercises and tracking/gamification elements. Participants valued the supportive information for the exercises including being able to watch a demo and explanation of each exercise prior to completing the workout. The other additional app features like goal tracking, music, and rewards were used less often by participants. Some participants liked these motivational features such as rewards, but most participants identified that these features might be helpful or motivating to other participants but described how they didn't use these features much. While this may have been due to the rewards section being a separate rather than integrated feature of the app, importantly, these features didn't interfere with their ability to use the app. One participant shared:

> "*I didn't look at what points I was earning or whatever trophies. It was a bit silly... So you know, there's just some things in the app that for me weren't necessary. The key thing was that my exercises were there, and I could access them... I didn't access most of the rest of the app... Maybe others find the motivation and so on more useful than I did*." (P8)

4.4.4 Sustainability

Participants valued the program and offered insight into how the program could continue moving forward. This was an unanticipated learning that was patient driven. This category

emerged in part from discussions at the end of interviews, when participants were asked if there was anything else they wanted to share. Participants saw this as an opportunity to bring up the future directions of exercise programming for people with MM. This wasn't a primary objective of the interviews but was a central component of the conversations because it was identified by participants as important.

Participants valued the program so much that they wanted it to continue, so that all people with MM have the opportunity to benefit from the program. This was demonstrated by participants continuing to access the program until the study was fully closed, even after their initial 12-week commitment was complete. They explained that there are no other programs that are myeloma-specific available to them. Therefore, this program is important because it fills a current gap in care. Many participants recognized that for this to continue, it needed to be transitioned from a study into a program. As one participant shared, they hoped "*this leads to something that becomes available outside of a research study just as a tool for myeloma patients and others to use*" (P8).

Participants even shared ideas for how to deliver and/or fund the program in a sustainable way. For example, they suggested partnering with the local cancer centre and survivorship centres for referrals and delivery and partnering with the local myeloma support society for funding/fundraising. Indeed, it seemed that participants felt that securing dedicated funding was essential for long-term sustainability. Some participants offered to engage with funders and government officials to support efforts to secure dedicated funding. One participant said:

> "*If funding were an issue, that would be something we could bring up with the local myeloma group. Address it with them. And there could be some fundraising or, you know, maybe you had to buy the app or something like that. Definitely, rather than, you know, kind of dropping the app completely because of funding, it would be nice to know ahead of time. Okay, we can continue this if we had so many dollars, so that would be nice. I mean, I can't see the government. Well, I can see it, but it's definitely they're going to get their money back. Because anyone, especially our cancer patients, right now, if you're more fit then you're less likely to end up in the hospital, right? So, for sure, you're going to see the cost there*" (P30).

4.5 DISCUSSION

The aim of this study was to determine both participants' overall perceptions and perceptions of the strength and limitations of a virtually-supported home exercise program and eHealth application. Participants had positive perceptions of the exercise program. Supportive and responsive programming was seen as a key strength by participants, as they valued that the program was individually-tailored and was adjusted through active support from knowledgeable and empathetic personnel. They also valued that the program offered diverse exercise opportunities including both live group and independent home workouts, so they could take part in the exercise format they enjoyed most. Participants felt the app was user friendly, but certain aspects of the app were less intuitive and could be revised. Finally, participants wanted the study to transition into a program and thought that partnering with local cancer centres, survivorship centres, and patient support groups could facilitate sustainable program referral, delivery, and funding.

4.5.1 One Size Does Not Fit All

To our knowledge, this is the first independent qualitative study on the acceptability of a myeloma-specific exercise program. This study affirms that one size does not fit all when it comes to exercise programming in MM. Instead, programming should be supportive and responsive to the needs of participants. This supports previous qualitative research, where people with MM identified individualization as a key program characteristic due to the side effects from MM and MM treatments and differences in exercise experience (73). Indeed, a recent review of the effectiveness of exercise in MM proposed tailoring as fundamental for exercise programs in this population (74). The current study expands on these previous studies by identifying strengths beyond tailoring that contributed to this program's supportive and responsive nature. Specifically, active support through one-on-one check-ins provided a structured opportunity to modify programming and correct exercise technique. Active support may be of particular importance for home programs, where interaction between the exercise specialist and the participant is often limited. Participants also felt the program was delivered by appropriate personnel (i.e., a kinesiologist with > 3 years of experience working with the population overseen by a physical therapist with > 20 years of experience in cancer rehabilitation, a certified exercise physiologist, and a hematologist/oncologist). Above all, having qualified personnel

delivering the program instilled trust and confidence in participants. They trusted they were in the right hands and were confident that the exercises they were performing were safe. This is likely important because fear of injury, lack of confidence, and lack of knowledge are all patient-reported barriers to exercise in MM (70). Tailoring, active support, and appropriate personnel cannot completely eliminate the risks of exercise in this population (Chapter 3). However, a supportive and responsive program that employs these strategies can form a safety net around the participant, making exercise safer and more comfortable.

Results from this study also suggest that programs should offer diverse exercise opportunities. Indeed, previous research suggests that participants think programs should be individualized based on exercise preference (73). In the context of the current study, offering a combination of live group classes and independent home workouts was seen as a strength, as the two methods of delivery complemented each other, each with their own benefits. The group classes allowed participants with MM to interact with each other, despite being in a home program. This social aspect may be of particular benefit, as greater improvements in quality of life have been seen from group exercise than from personal training in other tumour groups (119). The current study's group classes also created an opportunity for participants to receive supervision and feedback while exercising at home. Exercise supervision has been proposed as a contributor to program success in MM (74) and is favoured by some people with MM (73). Indeed, some participants in the current study felt the group class was a safer exercise environment for them. However, people with MM have also identified the importance of flexibility in exercise programming (73). This highlights the value of independent home workouts, as participants in the current study valued the flexibility of this exercise format. Importantly, neither option was universally regarded by participants as superior. Future programs should aim to include diverse program options, such as live group classes and independent home workouts, to leverage the benefits of different exercise formats and/or to match participants with the exercise format that aligns with their preferences.

4.5.2 App Usability

To our knowledge, this is the first study to employ an eHealth application to deliver exercise programming in MM. The HEAL-Me App appears to be an acceptable eHealth application for this population. Participants described the app as user friendly and simple, despite

generally not having much experience with technology. However, it appears that certain areas of the app should be revised so participants can more easily log their workouts, so their exercise progress is more reliably reflected on the participant-facing side, and so the app runs smoother to avoid app stalls and slow responses. One of the primary strengths of the HEAL-Me App was the ability for participants to follow along to exercise videos containing demonstrations, explanations and cueing as they completed their independent home workouts. This is a recommended format for home exercise delivery, as it allows the exercise specialist to provide high quality, engaging exercise guidance for people living with cancer, at home (107). The virtual/eHealth delivery was also valuable because most people with MM are immune compromised and are therefore at an increased risk of infection. This model of delivery was thus particularly important during the COVID-19 pandemic, but may also have a role in the future, as risk of infection is a previously reported barrier to exercise in this population (71). Participants had varying perspectives on the app's gamification components, including rewards, achievements, and goal tracking. Although some participants thought these components were strengths, most participants thought they could be of benefit to others but were not relevant or needed for themselves. These gamification components may not be necessary for some given that many older adults are primarily motivated by intrinsic factors, such as the health benefits of exercise and feeling better (120). If these features are included in eHealth apps, they should not interfere with the app's primary purpose of delivering exercise programming. Above all, the chosen application should be simple and easy to use for the patient population (121).

4.5.3 Sustainability

An unanticipated learning from the interviews was the importance of sustainability for participants. Participants valued the program and experienced diverse program benefits, so they wanted the study to transition into a program that they and other people with MM could access going forward. Indeed, there are no equivalent programs for people with MM in Alberta. The lack of programs for people with MM may be due, at least in part, to the need for specialized programming to manage their symptoms and risk. Many programs may not have sufficient resources and trained personnel to deliver appropriate programming for this population. Participants in this study felt that if exercise is beneficial, efforts should be made to ensure they have access to exercise programming that supports them beyond a 12-week study period. The

transition from research study to established program is a common stalling point in the field of exercise oncology and most studies do not discuss program sustainability (122). Participants in this study identified partnerships with local organizations/hospitals and securing funding as two ways to potentially help this transition, which aligns with previous research (122, 123). As a whole, these findings provide our research team with guidance moving forward. Firstly, more research is needed to understand what conditions are needed to facilitate a successful transition of exercise programming into practice. Additionally, our research team will continue to involve people with MM as partners in research, to co-design sustainable programs that meet the needs of participants. In our case, partnering with the local survivorship centre or embedding a myeloma-specific stream of programming into an on-going program currently being implemented into care (76) seem promising as they both already have infrastructure to offer programming. In both cases, a final step would be to ensure funding and appropriate personnel are secured. A long-term program of this sort is warranted in this population, given that ongoing support is likely needed as people with MM move through their myeloma journey, experiencing relapse, recurrence, and changes in symptoms.

4.6 CONCLUSION

The virtually-supported home exercise program was acceptable for people with MM. A key strength of the program was its supportive and responsive nature, involving individually-tailored programming that was adjusted through active support and delivered by a multidisciplinary team of appropriately trained personnel. This model should be used in future research to create an exercise safety net for participants to minimize and manage the potential risks of exercise in this population. Future studies should also aim to include diverse exercise opportunities, as participants identified this as a strength of the program. This allows researchers to leverage the benefits of both group classes (i.e., supervision) and independent workouts (i.e., flexibility) and ensure programming can match the preferences of participants. The eHealth application used to deliver the program (HEAL-Me) is acceptable for use by people with MM. Participants described the app as simple and user friendly. The app also allowed the intervention to be delivered entirely in a remote format, which is of particular benefit given that most people with MM are immunocompromised. Finally, participants felt the program was limited as it did not continue after the 12-week study period. Given that participants saw sustainability as a

priority, involving people with MM as partners in future research aiming to create sustainable programs that meet the needs of people with MM is recommended.

CHAPTER 5: DISCUSSION

This thesis discusses the feasibility, acceptability, and preliminary efficacy of a tailored, virtually-supported home exercise program for people with MM. To our knowledge, this thesis contains both the first eHealth-based exercise program for people with MM and the first independent qualitative study on the acceptability of a myeloma-specific exercise program. Important learnings from this thesis include: (1) exercise safety, (2) preliminary findings of benefit, (3) delivery mode, and (4) sustainability.

5.1 Exercise Safety

No serious adverse events (grade ≥ 3) occurred in this study. However, there was a higher than anticipated rate of musculoskeletal events observed in this study. This contrasts with several previous studies in MM, which either failed to report on adverse events (18, 20, 62) or reported that no adverse events related to the intervention occurred (15, 16, 19, 21). Evaluating the exercise prescriptions employed in some of these studies (18-20, 62), it's possible that adverse events did not occur because the exercise programs were underdosed, from fear of participants experiencing fractures (70). Indeed, several studies excluded participants with bony disease (15, 16, 21, 68), those who are likely at higher risk of events. Delivering a lower intensity intervention to people with MM who also have less advanced disease may help to avoid adverse events, but these interventions risk not leading to meaningful changes in physical function and quality of life. They also ignore a significant proportion of the MM population, limiting generalizability. A recent meta-analysis found that exercise increases participants' risk of non-serious adverse events but does not increase risk of serious adverse events (95).This meta-analysis included participants both with or without medical conditions but excluded participants receiving chemotherapy, so it remains unclear how exercise might modify the risk of adverse events in MM.

It is likely not possible to completely eliminate the potential for an increased risk of adverse events in a sufficiently dosed exercise program in this population. Researchers should thus anticipate a greater rate of adverse events, as well as unique challenges in prescribing exercise to participants with MM. For example, the adverse events in the current study were related to exercises involving either core strain or dynamic movement. Core strengthening is

likely important for people with MM (102-104), but may put strain on the spine and/or lesion sites. These exercises should be individually tailored to the participant with consideration given to positioning as well as loading forces on the spine to minimize the risk of causing or worsening existing back pain, as observed in this study.

Researchers should strive to create a safety net that aims to minimize the likelihood and severity of events by delivering individually-tailored programming, offering supervision and active support to participants, and ensuring programming is delivered by trained and experienced personnel. Although previous studies in MM have claimed to have tailored exercise programming, this study is the first to systematically track how the program was tailored to each individual. Each participant's program was built from a myeloma-specific developed protocol that was further adapted on a weekly basis to ensure programming was appropriate for them. Specifically, programming was adapted on an individual basis to manage symptoms and conditions like myeloma-related pain and history of fractures/lytic lesions in an area, which are common barriers to exercise for people with MM (70, 71). We believe that in the absence of these purposeful program changes, the program may not have been tolerated as well by participants. Indeed, a central finding from this thesis is that one size does not fit all in exercise prescription for people with MM. Participants felt that the program should be supportive and responsive to their needs by including program tailoring. This aligns with findings from a previous qualitative study in MM (73).

Supervision was included in this study, which is a program feature not often included in home programming (74). This was done because supervision has been proposed to enhance effectiveness and appropriateness of programming for people with MM (74) and it appears that exercise programs that are supervised are more effective that unsupervised programs for people living with cancer (13). In this study, supervision involved weekly supervised one-on-one or small group workouts and regular one-on-one check-ins between the participant and exercise specialist. Supervision was likely important for program feasibility as it gave the exercise specialist the opportunity to provide tailored feedback to participants about their form and fostered discussions that informed program adaptations and advice/support provided by the exercise specialist. Participant perceptions of the program validate this, as they identified active support through the check-ins and group workouts as a key strength of the program.

Additionally, this program was delivered by a team of well trained and experienced exercise and oncology professionals. Exercise prescription was led by a kinesiologist with years of experience prescribing exercise to people living with advanced cancers. This is a key asset of this program, as most programs for people living with cancer would have staff with lower level credentials (122). Personnel was an important strength of the program in the eyes of the participants. They emphasized that having qualified and empathetic personnel instilled trust and confidence in them. This helped them feel more comfortable exercising. It is recommended that future studies consider using highly trained/skilled personnel capable of developing a strong therapeutic relationship with participants, similar to the current study, to deliver exercise programming for MM to ensure participants can exercise safely.

5.2 Preliminary Findings of Benefit

Participants experienced promising changes over the course of the 12-week program, which warrant further investigation in a randomized controlled trial. Specifically, significant improvements in leg strength, core strength, and balance were observed in this study. Maintaining and improving leg strength in MM is important, given the deleterious impacts of prolonged corticosteroid use on proximal muscle strength (4, 79) and the link between lower extremity muscle weakness and fall/fracture risk (97, 98). Similarly, maintaining and improving core/back strength is important, given that core strength is associated with dynamic balance and that back strengthening can reduce axial deformity (103), reduce chronic back pain (3), and prevent vertebral fractures (104). Finally, the improvements in balance are meaningful, given the link between fall risk and fracture risk in MM (98). Taken together, improvements in these outcomes can lead to decreased pain (3), improved posture (103), decreased fracture risk (104), decreased mortality, and decreased hospital costs (100, 101). The additional physical improvements observed in this study, including aerobic capacity and flexibility, will also contribute to the improved function of people with MM. Future studies should consider including individually-tailored exercises that specifically target these fitness components and ensure they include outcome measures that can capture changes in these components.

In addition to changes in physical function, significant improvements in quality of life and physical symptom burden were observed in this study. Given that people with MM generally experience a high symptom burden and low quality of life (105), these findings warrant further

investigation. Interestingly, no changes in fatigue were observed in this study, and psychological symptom burden worsened over the course of the program. This contradictory finding may be explained by the context the study was conducted within. Specifically, the COVID-19 pandemic has significantly increased the incidence of anxiety and depression amongst people living with cancer (106), and it's possible that the heightening risk of infection and changes in public health measures over the course of the program influenced participants' feelings of anxiety and depression. Importantly, total symptom burden was maintained over the 12-weeks, which is important, given the progressive nature of MM. These findings suggest that there may be significant benefit from exercise for both the physical function and quality of life of people with MM, despite having a higher than normal risk of musculoskeletal events. Furthermore, longer term follow up could provide further indications of what the lasting impacts of the program might have been. Further research is warranted to investigate the impact of exercise of quality of life, symptom burden, and fatigue in people with MM.

5.3 Delivery Mode

The virtual delivery of the program was acceptable for people with MM. Participants had positive perceptions of the program and reported that the program lessened their feelings of isolation, improved how they felt, and allowed them to realize benefits specific to their disease and treatments, including improved core strength, back strength and balance. These findings support findings from Chapter 3, which found improvements in core strength and balance over the course of the program.

To our knowledge, this is first study to date that has employed an eHealth application to deliver exercise programming in MM. Given this, an important finding from Chapter 4 was that the HEAL-Me App appears to be an acceptable eHealth application for this population. Participants felt that the app was user friendly, easy to use, and useful for them to complete the exercise program. This aligns with satisfaction survey results from Chapter 3, where participants reported that both learning how to use HEAL-Me and actually using HEAL-Me were not burdens. However, participants highlighted a few sections of the app that were less user friendly and/or contained glitches. Interestingly, participants often qualified these comments by explaining their lack of technology experience. Participants felt that the issues they encountered were because of their own inexperience, as opposed to issues with the app itself. Importantly, the

issues they highlighted did not impair their ability to use the application to exercise. Beyond being user friendly, the eHealth application had a few key strengths. First, it allowed for participants to complete their home workouts through an engaging follow-along video format that contained demonstrations, explanations, and cueing. This format of delivery enables specialists to provide high quality, engaging exercise guidance for people living with cancer, at home (107). Secondly, the eHealth application and the virtual delivery of the exercise program was seen as valuable because it decreased participants' risks of infection. This was particularly important in the context of the COVID-19 pandemic, given that most people with MM are immunocompromised. Interestingly, risk of infection is a previously reported barrier to exercise in this population (71), so there is likely utility for virtually delivered programming in the future as well.

The HEAL-Me App also allowed for seamless delivery of diverse exercise formats of exercise (i.e., both live group classes and independent home workouts). Participants thought that offering a combination of live group classes and independent home workouts was a strength, as the strengths of the two methods complemented each other. Participants reported that the group classes allowed them to interact with other participants. Indeed, the added interaction from this format may contribute to greater improvements in quality of life than from personal training (119). Another main strength of the group classes was the built-in opportunity for supervision and immediate feedback on exercise performance. As described earlier, supervision has been proposed as a contributor to program success in MM (74) and is favoured by some participants (73). Given the benefits of group classes, future programs should aim to include a similar format of exercise that allows for interaction between participants and the opportunity for direct supervision and feedback from the exercise specialist. However, participants also identified several strengths of the independent home workouts that cannot be ignored. Specifically, participants felt the independent workouts were flexible, allowing them to complete them whenever it was convenient for them. This aligns with previous research, where people with MM identified the importance of flexibility in exercise programming (73). Future programs should aim to include multiple program options to leverage the benefits of each exercise format (i.e., group classes for interaction and supervision, independent home workouts for flexibility) and/or to match participants with the exercise format that aligns with their preferences.

It was unclear whether the gamification and tracking components of the app were necessary in this population. Some participants valued these components to keep them accountable and engaged, but many participants thought they may be of benefit to others but were not necessary for themselves. Many older adults and people with chronic disease are primarily motivated to exercise by intrinsic factors, such as feeling better (120), which may explain why many participants felt these external motivators were not relevant for themselves. More research is warranted to investigate whether gamification/tracking components are of benefit and interest for people with MM and if so, what strategies might be optimal. Future researchers should ensure that the eHealth application they choose to deliver their exercise programming is simple and easy to use for the patient population.

5.4 Sustainability

The final key learning from Chapter 4, which was unanticipated, was the importance of sustainability for participants. Participants' positive experiences in the program made them want the study to transition into a program so they and others could access the program going forward. People with MM have unique exercise needs and represent a small proportion of the cancer population, so there are no equivalent programs in existence for people with MM in Alberta. It was interesting that participants brought this topic up in the interviews unprompted, as the transition from research study to established program is a common stalling point for exercise studies in oncology. Indeed, most studies do not discuss program sustainability (122). Participants even identified ways to transition the study into a program that align with previous research on the sustainability of exercise programming. Specifically, participants identified partnerships with local organizations/hospitals and securing funding as two ways to potentially help this transition, which aligns with a recent review (122). Additionally, the inclusion of cost-effectiveness analyses in exercise studies may be key in convincing policy makers to provide long-term funding for exercise programs for people living with cancer (122). More research is needed to understand what conditions facilitate a successful transition of exercise into practice. Future researchers should work with people with MM to co-design programs that can meet the needs and priorities of participants. Researchers should also investigate potential partnerships that could facilitate the sustainability of programming beyond the duration of the initial study.

5.5 Limitations

This thesis has some limitations that should be identified. Firstly, this is a single group study. Without a control group, it is not possible to distinguish between the effect of the treatment (exercise), a placebo effect, and the effect of time. This design was chosen due to the study's primary focus on feasibility. Feasibility was the primary focus of this study given the inconsistency of results from previous research in MM and the fact that it is still not clear whether virtually-delivered programming is safe in this population. The effects of this exercise program on physical function and quality of life should be confirmed by a randomized controlled trial to discern whether the changes observed in the current study can be attributed to the exercise program itself. Secondly, gold standard measures of fitness were not used. Gold standard assessments are the most accurate method of determining fitness but require significant equipment and participant attendance at a testing facility. This creates a barrier for people living with cancer in rural/remote communities. Additionally, delivery of in-person assessments was not possible at several timepoints over the last year due to the COVID-19 pandemic. To minimize the risk of viral transmission and reach participants from a wider catchment area, remote fitness assessments were conducted. Importantly, the selected assessments have established validity and reliability and were completed by trained personnel. Lastly, the impacts of the COVID-19 pandemic may limit the generalizability of the findings from the current study. COVID-19 has had a significant impact on the psychological health of people living with cancer (106), and the public health measures in place to limit disease transmission have changed how people spend their day. This may have influenced results, as participants might have had more time/energy to dedicate to exercise, given that certain activities and destinations were inaccessible to participants during this time.

5.6 Conclusions & Future Directions

This thesis supports the feasibility and acceptability of a 12-week virtually-supported home exercise program for people with MM. Although feasible, researchers should anticipate a higher rate of adverse events in this population and should ensure they monitor for, record and are prepared to respond to events. Programming should be individually-tailored and include supervision, active support, and well-trained and empathetic personnel to manage participants' risk of musculoskeletal events and create a comfortable environment for participants to exercise.

Programming should also include multiple delivery formats to leverage the benefits of both supervised and unsupervised exercise. The eHealth application used to deliver the program was acceptable for use by people with MM. eHealth applications should be user friendly, easy to use, and useful to participants for completing home exercise. Additional application features like gamification and tracking may be of benefit to some participants but should not impair participants' ability to use the app to complete their exercise program. A large scale randomized controlled trial is warranted to confirm the effects of the current exercise program on outcomes including leg strength, core strength, balance, quality of life, and symptom burden. Given the challenges of living with MM, involving people with MM as research partners may better inform the design of sustainable programs that meet the needs and priorities of the patient population.

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APPENDICES

Appendix A: Consent Form and Addendum

Informed Consent Form for Participation in a Research Study

Feasibility of a Virtually Supported Home-Based Resistance and Aerobic Exercise Program for Cancer Survivors with Multiple Myeloma

Myeloma Progressive Resistance and Aerobic Exercise Study (MY PROGRESS)

Protocol ID: *HREBA.CC-20-0201*

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

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

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

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

Taking part in this study is voluntary. You may choose not to take part or, if you choose to participate, you may leave the study at any time without giving a reason. Deciding not to take part or deciding to leave the study will not result in any penalty or any loss of medical or health-related benefits to which you are entitled. The principal investigator, who is one of the researchers, will discuss this study with you and will answer any questions you may have. If you do consent to participate in this study, you will need to sign and date this consent form. You will receive a copy of the signed form.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

Multiple myeloma and myeloma treatments take a toll on the body, mind, and overall health of survivors. Exercise can improve the health and wellbeing of cancer survivors. However, it is still not clear what kind and amount of exercise is best for cancer survivors with multiple myeloma. The Health Research Ethics Board of Alberta – Cancer Committee (HREBA-CC), which oversees the ethical acceptability of research involving humans, has reviewed, and granted ethics approval for this study.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to measure the safety and feasibility of a virtually supported home-based exercise program for cancer survivors with multiple myeloma. The program is called the Myeloma Progressive Resistance and Aerobic Exercise Study (MY PROGRESS). Our aim is to support persons who have been diagnosed with multiple myeloma to adopt an active lifestyle to improve their health.

WHAT ARE OTHER OPTIONS IF I DECIDE NOT TO PARTICIPATE IN THIS STUDY?
You do not have to take part in this study to receive continued medical care. You may choose not to participate in this study. Your healthcare provider will discuss lifestyle recommendations with you. Right now, the usual treatment at the Cross Cancer Institute is to receive counseling on the value of physical activity and healthy living after the completion of cancer treatments.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Up to 25 people with multiple myeloma across Alberta will take part in this study.

WHAT WILL HAPPEN DURING THIS STUDY?
STUDY INTERVENTION
If you agree to take part in this study, you will undergo screening and fitness testing before beginning the exercise program. The exercise program will use an online application (app) to support you exercising at home. You will take part in an exercise program 2-3 times per week for a 12-week period. The exercise program will be designed based on your fitness level and your fitness or lifestyle goals. Before the program starts, you will be shown the app and will be trained how to use it. Your program will involve a combination of independent exercise sessions prescribed to you by the study team and virtual (live) exercise sessions run by the research team. Sessions will involve aerobic, resistance, balance, and flexibility exercises. The study team will check-in with you on a regular basis over the 12-weeks to make sure the program is safe, enjoyable, and appropriate for you. You will need a piece of technology (like a smartphone, tablet, or computer) and access to the Internet to complete the sessions.

All participants will have measurements taken at the start of the study which will be compared with measurements taken at the end of the program (12 weeks later) to see the effect of exercise on physical activity levels, fitness, and quality of life.

STUDY PROCEDURES
Fitness Tests
The following tests will be done as part of this study. Testing will be done virtually using video conferencing software (Zoom). You will need a piece of technology (phone, computer, tablet), a camera, and connection to the internet for the testing. If the results show that you are not able to continue participating in the study, the principal investigator will let you know.

- Body composition measurement: We will have you measure your height and body weight if you are able. These measurements take between 2 and 3 minutes to complete.
- Aerobic endurance measurement: We will have you perform a 2-minute step test on a flat surface to determine your fitness level. You will walk at a moderate pace for the 2-minute period. The step test takes around 5 minutes to complete.
- Musculoskeletal fitness measurement: we will measure your lower body endurance (30s Sit to Stand), and assess your flexibility using a sit-and-reach test and shoulder elevation measure. We will assess your core endurance (plank test). We will also assess your balance using a one-legged stance balance test. These tests take 20 minutes to complete.
- Optional fitness tests: Depending on your interests and your location of residence, you may have the option to undergo additional fitness testing in person. This testing could include any of the following: a moderate aerobic endurance test; additional body measurements (height, weight, waist and hip circumference); maximal strength test for your arms (bench press) and your legs (leg press); grip strength; fall risk (3 meter backwards walk)

Questionnaires
You will be provided with a questionnaire package at the start of the study and at 12 weeks. The purpose of the questionnaires is to understand how the program affects different aspects of your life.

- Screening and identifying information forms (at the start of the study only): you will be asked to fill out a few questionnaires that provide us with important medical information to ensure this study is safe for you. You will also fill out an identifying information form, so we are able to contact you. These screening questionnaires take 10 minutes to complete.
- Exercise preferences questionnaire (at the start of the study only): This questionnaire asks about your exercise goals and the type of exercises you would like to take part in. This questionnaire takes 1 minute to complete.
- The revised Edmonton Symptom Assessment Scale: this questionnaire asks you to rate symptoms related to your cancer and cancer treatment. This questionnaire is usually administered as part of your standard care. This questionnaire takes about 5 minutes to complete.
- Physical activity level: We will ask you about your physical activity level using the Godin Exercise Leisure-time Questionnaire. This 6-item questionnaire asks specific questions about the type, intensity, frequency, and duration of your average weekly physical activity. This questionnaire takes around 2-3 minutes to complete.
- Cancer-related Quality of Life: We will assess your quality of life using the Functional Assessment of Cancer Therapy-Multiple Myeloma and Fatigue Scale. This 51-item questionnaire asks specific questions about the impact of your cancer and cancer treatment on your wellbeing and fatigue. This questionnaire takes around 10 minutes to complete.
- Bone pain & neuropathy: these myeloma and myeloma treatment side effects will be measures using the Bone Pain and Neurotoxicity subscales of the Functional Assessment of Cancer Therapy system. These questionnaires take around 5 minutes to complete.
- Upper extremity function: we will assess your upper body function using the 20-item Upper Extremity Functional Index. This questionnaire asks you questions about how well you can do activities of daily living that use your upper body.
- Lower extremity function: we will assess your lower body function using the 20-item Lower Extremity Functional Scale. This questionnaire asks you questions about how well you can do activities of daily living that use your lower body.

The information you provide is for research purposes only and will remain strictly confidential.
Some of the questions are personal; you may choose not to answer them. Even though you may have provided information on a questionnaire, these responses will not be reviewed by individuals not involved in this study, e.g., your health care practitioner/team. If you would like them to know this information, please bring this to their attention.

Participant Diaries

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

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

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

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

The main risk associated with exercise is musculoskeletal injury (injury to the muscles, tendons, joints, or bones). Your exercise sessions will be supported, and your program designed to minimize this risk by slowly increasing the amount and intensity of your exercise over time.

There is also a very small risk of heart issues (such as chest pain, irregular heart rate, heart attack) should you exercise too intensely. To avoid any risks associated with exercise, you will be screened to ensure it is safe and appropriate for you to take part in the exercise program. All exercise will be of a low to moderate intensity level to minimize the stress on the heart and body. As well, we will ask you to check your heart rate and blood pressure before and after the exercise testing and if needed, when you exercise at home. Multiple myeloma can increase your risk of fracture. To minimize the risk that you break a bone while exercising, your exercise program will be tailored to your condition, and movements that may put you at risk (e.g. twisting, hard balancing exercises, or heavy loads) will be avoided.

If any concerns are identified at any time, you will be referred to your doctor for further evaluation. If any issues develop during the study period, your exercise sessions may be held or discontinued. If you have any side effects, you should call the principal investigator or study coordinator in charge of the study. The telephone numbers are on the last page of this form.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?
Participation in this study may or may not be of personal benefit to you. Possible benefits include improved physical fitness and better energy.

WHAT ARE MY RESPONSIBILITIES AS A STUDY PARTICIPANT?
If you choose to participate in this study, you will be expected to:

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

HOW LONG WILL I BE PARTICIPATING IN THIS STUDY?
The exercise program will last for 12 weeks. You will be asked to complete a follow-up assessment and questionnaires at 12-weeks. No further follow-up is required.

WILL THERE BE ANY LONG-TERM FOLLOW-UP INVOLVED WITH THIS STUDY?
If you stop receiving the study intervention early, we would like to keep track of your health for 12-week period to look at the effects of the exercise intervention on your health. We would do this by having you complete the follow-up fitness assessment and/ or by completing the questionnaire.

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

or using other private sources of information, is optional; please indicate your decision using the check boxes below.

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

☐ Yes ☐ No Participant's Initials: _____

Name/phone number of care physician: _____

CAN I CHOOSE TO LEAVE THIS STUDY EARLY?

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

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

CAN MY PARTICIPATION IN THIS STUDY END EARLY?

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

- You are unable to tolerate the exercise.
- You sustain an injury because of participation.
- You experience an adverse effect during or after exercising.
- Your doctor no longer feels this is the best treatment for you.

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

HOW WILL MY PERSONAL INFORMATION BE KEPT CONFIDENTIAL?

If you decide to participate in this study, the principal investigator and study staff will only collect the information they need for this study. Records identifying you, including information collect from your medical files/records, such as your Electronic Medical Records (EMR), Netcare, charts, etc., will be kept confidential to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

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

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

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

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

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during the study will be used in analyses and will be published and/or presented to the scientific community at meetings and in journals, but your identity will remain confidential. It is expected that the study results will be published as soon as possible after completion.

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

Data collected will be entered into the secure REDCap server held at the University of Alberta and data will only be used for research purposes. Data will be kept for a minimum of 5 years following completion of the study. Hard copies of data will be shredded as per organizational procedures. Studies involving humans sometimes collect information on race and ethnicity as well as other characteristics of individuals because these characteristics may influence how people respond to different interventions. Providing information on your race or ethnic origin is voluntary.

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

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

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

You will not have to pay for the exercise program you receive in this study. Access to the online application and on-going exercise support over the 12-week intervention will be of no cost to you. We will provide a parking pass to cover your parking cost if you attend optional in-person tests or procedures. There may be additional costs to you for taking part in this study if you choose such as:

- technology (phone/tablet/computer, camera, internet)
- transportation (if you attend in-person testing or procedures)

WILL I BE COMPENSATED FOR PARTICIPATING IN THIS STUDY?

You will not be paid for taking part in this study. However, in the case of research-related side effects or injury, as a direct result of participating in this research, you will receive all medical treatments or services recommended by your doctors. Although no funds have been set aside to compensate you in the

event of injury or illness related to the study treatment or procedures, you do not give up any of your legal rights for compensation by signing this form.

WHAT ARE MY RIGHTS AS A PARTICIPANT IN THIS STUDY?
You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study. You have the right to be informed of the results of this study once the entire study is complete. If you would like to be informed of these results, please contact the principal investigator. The results of this study will be available on a clinical registry; refer to the section titled "Where can I find online information about this study?". Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.
By signing this form you do not give up any of your legal rights against the hospital, investigators, sponsor, involved institutions for compensation or their agents, nor does this form relieve these parties from their legal and professional responsibilities.

IS THERE CONFLICT OF INTEREST RELATED TO THIS STUDY?
There are no conflicts of interest declared by the researchers of this study.

WHAT IF RESEARCHERS DISCOVER SOMETHING ABOUT ME AS A RESEARCH PARTICIPANT?
During the study, the researchers may learn something about you that they did not expect. For example, the researchers may find out that you have another medical condition. If any clinically important information about your health is obtained as a result of your participation in this study, you will be given the opportunity at that time to decide whether you wish to be made aware of that information.

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

The study registration number to use this website is: NCT04484714

WHO DO I CONTACT FOR QUESTIONS?
If you have questions about taking part in this study, or if you suffer a research-related injury, you should talk to the project coordinator or principal investigator. These person(s) are:

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

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

If you have questions about your rights as a participant or about ethical issues related to this study and you would like to talk to someone who is not involved in the conduct of the study, please contact the Office of the Health Research Ethics Board of Alberta – Cancer Committee at: 780-423-5727 or 1-877-423-5727 (Toll Free).

SIGNATURES

Part 1 - to be completed by the potential participant.

	Yes	**No**
Do you understand that you have been asked to take part in a research study?	☐	☐
Do you understand why this study is being done?	☐	☐
Do you understand the potential benefits of taking part in this study?	☐	☐
Do you understand the risks of taking part in this study?	☐	☐
Do you understand what you will be asked to do should you decide to take part in this study?	☐	☐
Do you understand the alternatives to participating in this study?	☐	☐
Do you understand that you are free to leave the study at any time, without out having to give reason and without affecting your future health care?	☐	☐
Do you understand who will see your records, including health information that identifies you?	☐	☐
Do you understand that by signing this consent form you are giving us permission to access your health information if applicable?	☐	☐
Do you understand that by signing this consent form that you do not give up any of your legal rights?	☐	☐
Do you understand that your family doctor/health care provider will/may be informed of your participation in this study?	☐	☐
Have you had enough opportunity to ask questions and discuss this study?	☐	☐

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

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

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

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

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

Signature of Person Conducting the Consent Discussion	PRINTED NAME	Date

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

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

Signature of Impartial Witness/Interpreter	PRINTED NAME	Date

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

ADDENDUM TO PARTICIPANT INFORMATION & CONSENT

Feasibility of a Virtually Supported Home-Based Resistance and Aerobic Exercise Program for Cancer Survivors with Multiple Myeloma: Exit Interview

Myeloma Progressive Resistance and Aerobic Exercise Study (MY PROGRESS)

Protocol ID: *HREBA.CC-20-0201*

Principal Investigator: Dr. Margaret McNeely, PT, PhD

Department of Physical Therapy/ Department of Oncology

University of Alberta & Cross Cancer Institute

Phone: 780-248-1531

Research/Study Coordinator: Graeme Purdy, BSc

Before beginning the Myeloma Progressive Resistance and Aerobic Exercise Study (MY PROGRESS), you signed an Information & Consent Form describing MY PROGRESS and your rights as a participant. At that time, it was explained that you would be informed of any changes to the study. If after discussing the new information with the coordinators, you would like to take part in this optional component of the study, please sign this Consent Form Addendum. The original consent formed, signed at the beginning of the study, is still applicable above and beyond the information contained in this addendum.

Optional component (one time only):

Post-MY PROGRESS Interview: As you have now finished the MY PROGRESS study, you have the option to take part in a semi-structured exit interview where we will ask you questions about your experience with the exercise program and the exercise application (HEAL-ME). The interview will take approximately 30 minutes to complete and will be conducted either through Zoom video conferencing or over the telephone. The information collected from the interview will help to inform both future exercise programming for cancer survivors with multiple myeloma and needed modifications to the HEAL-ME exercise application.

ADDENDUM TO CONSENT FORM

Title of Study: Feasibility of a Virtually Supported Home-Based Resistance and Aerobic Exercise Program for Cancer Survivors with Multiple Myeloma

Principal Investigator: Margaret McNeely, PT, PhD – 780-248-1531

Research/Study Coordinator: Graeme Purdy, BSc – 780-492-6007

I understand and appreciate the new information in this addendum concerning the study I already consented to participate in.

I have been given the opportunity to discuss the information contained in this addendum. All of my questions have been answered to my satisfaction.

This signature on this Information & Consent Form Addendum means that I agree to complete the optional component. I understand that I remain free to withdraw at any time.

Signature of Participant	Name (Printed)	Date

Signature of Person Obtaining Consent	Name (Printed)	Date

A SIGNED COPY OF THIS ADDENDUM MUST BE GIVEN TO THE RESEARCH PARTICIPANT

Appendix B: Ethics Approval

Health Research Ethics Board of Alberta
Cancer Committee
1500, 10104 - 103 Avenue NW
Edmonton, Alberta, T5J 0H8
Telephone: (780) 423-5727
Fax: (780) 429-3509
Email: cancer@hreba.ca

Certification of Ethics Approval

This is to acknowledge that the following research has been reviewed and on behalf of the Health Research Ethics Board of Alberta (HREBA) – Cancer Committee (CC) I am granting approval for your site's participation in the research.

Ethics ID:	HREBA.CC-20-0201
Principal Investigator:	Margaret McNeely
Co-Investigator(s):	Christopher Venner
Student Co-Investigator(s):	Graeme Purdy
Study Title:	Feasibility of a Virtually Supported Home-Based Resistance and Aerobic Exercise Program for Cancer Survivors with Multiple Myeloma
Sponsor:	

Effective: 26-Aug-2020 **Expires:** 25-Aug-2021

Research reviewed at the HREBA - Cancer Committee full board meeting of 11 August 2020.

The following documents have been approved:

- MY PROGRESS Pamphlet, 1.0, July 7, 2020
- Consent Form, 2.0, August 17, 2020
- Functional Assessment of Cancer Therapy - General, 1.0, July 9, 2020
- PAR-Q+, 1.0, June 23, 2020
- Upper Extremity Functional Index, 1.0, June 23, 2020
- Medical Abstraction Form, 1.0, July 14, 2020
- Demographic and Identifying Baseline Forms, 1.0, July 14, 2020
- Medical Background and Cancer-Specific Screening Form, 1.0, July 14, 2020
- FACT-Bone Pain, 1.0, July 9, 2020
- FACT-Myeloma Subscale, 1.0, July 9, 2020
- Godin Leisure Time Physical Activity Questionnaire, 1.0, June 23, 2020
- Exercise Diary, 1.0, July 14, 2020
- FACIT Fatigue Scale, 1.0, June 23, 2020
- Satisfaction Survey, 1.0, July 14, 2020
- Edmonton Symptom Assessment Scale & Screening for Distress, 1.0, June 23, 2020
- Activities-specific Balance Confidence Scale, 1.0, July 9, 2020
- Neurotoxicity Scale, 1.0, July 9, 2020

- Lower Extremity Functional Scale, 1.0, June 23, 2020

This Committee is constituted and operates in accordance with the Alberta Health Information Act (HIA), the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2), Good Clinical Practice (GCP) Guidelines of the International Conference on Harmonization (ICH), Health Canada's *Food and Drug Regulations* (FDR), Part C, Division 5 and is registered with the U.S. Department of Health and Human Services (HHS), Office for Human Research Protections (OHRP), IRB # 00009687.

It is noted that the study team would like to access personal health information for the purposes of this research.

The committee has determined that consent must be obtained from participants for the disclosure of this information.

As a requirement of the HIA, if your study uses health information a copy of this certification will be sent to the Office of the Information and Privacy Commissioner (OIPC). Members of the HREBA-CC who are named as principal investigators or co-investigators in this research do not participate in discussions related to, nor vote on, such studies when they are presented to the Committee. The membership of this Committee is listed at www.hreba.ca.

This approval is subject to the following conditions:

1. It is being granted only for the research described in this application.
2. Any modification to the approved research must be submitted to the Committee for approval prior to implementation.
3. Reportable events (SAE's, new safety information, protocol deviations, audit findings, privacy breaches, and participant complaints) are to be submitted in accordance with the Committee's reporting requirements.
4. A request to renew this ethics certification must be submitted and reviewed by the Committee in advance of the expiry date indicated above. Failure to submit a request will result in the file entering into an expired state, whereby all research must cease.
5. A closure request must be submitted to the Committee when the research is complete or has been terminated.

This approval does not guarantee that you will be able to access health records for research purposes. Other institutional or organizational requirements may be in place that you will be required to meet prior to initiating your research. These include approvals for the allocation of resources in support of your study. Inquiries regarding these additional approvals should be directed to the appropriate institutional or organizational body.

Please accept the Committee's best wishes for success in your research.

Approved on behalf of CC by, Date:

Dale Dewhurst, Chair , HREBA-CC 26-Aug-2020

Note: This correspondence includes an electronic signature (validation and approval via an online system).

Health Research Ethics Board of Alberta
Cancer Committee
1500, 10104 - 103 Avenue NW
Edmonton, Alberta, T5J 0H8
Telephone: (780) 423-5727
Fax: (780) 429-3509
Email: cancer@hreba.ca

Modification of Ethics Approval

This is to acknowledge that the modification to the research indicated below has been reviewed and on behalf of the Health Research Ethics Board of Alberta (HREBA) – Cancer Committee (CC), I am pleased to advise that approval has been granted.

Ethics ID:	HREBA.CC-20-0201_MOD1
Principal Investigator:	Margaret McNeely
Co-Investigator(s):	Christopher Venner
Student Co-Investigator(s):	Graeme Purdy
Study Title:	Feasibility of a Virtually Supported Home-Based Resistance and Aerobic Exercise Program for Cancer Survivors with Multiple Myeloma

Sponsor:

Effective: 26-Aug-2020 **Expires:** 25-Aug-2021

Modification reviewed by delegated review on 13 January 2021.

The following documents have been approved:

- Consent Form Addendum, 1.0, January 11, 2021
- Patient Engagement Interview Guide, 1.0, January 11, 2021
- Proposal - Clean Version, 3.0, January 11, 2021

This Committee is constituted and operates in accordance with the Alberta Health Information Act (HIA), the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2), Good Clinical Practice (GCP) Guidelines of the International Conference on Harmonization (ICH), Health Canada's *Food and Drug Regulations* (FDR), Part C, Division 5 and is registered with the U.S. Department of Health and Human Services (HHS), Office for Human Research Protections (OHRP), IRB # 00009687.

Members of the HREBA-CC who are named as principal investigators or co-investigators in this research do not participate in discussions related to, nor vote on, such studies when they are presented to the Committee. The membership of this Committee is listed at www.hreba.ca. Please note that the approval of this modification does not change the effective or expiry dates of this study as indicated above. Please accept the Committee's best wishes for success in your research.

Approved on behalf of CC by, **Date:**

Raul Urtasun , HREBA-CC 14-Jan-2021

Note: This correspondence includes an electronic signature (validation and approval via an online system).

Appendix C: Eligibility Screening and Enrollment

Inclusion Criteria	
Is the participant over 18 years old?	○ Yes ○ No
Does the participant have a cancer diagnosis of multiple myeloma?	○ Yes ○ No
Which of the following treatment categories does the participant fall under? If unsure, enter details under "other" and discuss with study coordinator regarding participant's eligibility.	○ Transplant ineligible, currently in first line treatment ○ Transplant eligible patient, sufficiently recovered from transplantation (>3 months following transplantation) ○ Patient with relapsed/recurrent myeloma with either 1-3 prior lines or 4+ prior lines) ○ Other
Is the participant able to provide informed written consent in English?	○ Yes ○ No
Is the participant available to part in a 12-week exercise program at this moment?	○ Yes ○ No
Does the participant have internet access, a camera, and a device that would work to follow their program at home (e.g. laptop, desktop computer, smartphone, tablet)?	○ Yes ○ No
Exclusion Criteria	
Does the participant have one of the following diagnoses, in the absence of multiple myeloma: - AL amyloidosis - Solitary Plasmacytoma - Waldenstrom macroglobulinemia	○ Yes ○ No
Is the participant deemed to be too frail to partake in a home program based on red flags from the assessment (e.g. cannot perform 1 sit-to-stand or cannot balance for > 3 seconds on one foot)	○ Yes ○ No
Clearance & Final Decision	
Has physician approved been received for this participant to take part?	○ Yes ○ No
Have all eligibility conditions been met?	○ Yes ○ No

Appendix D: Program Intake Questionnaire

Program Intake Questionnaire

Cancer Diagnosis and Treatment	
What is the date of your initial diagnosis of cancer?	
What is the specific name of the myeloma/blood cancer you've been diagnosed with?	
Do you have bone involvement (i.e., bone lesions) related to your cancer?	o Yes o No o Unsure
Please identify the area of bone involved (e.g., pelvis, spine, etc.)	
Have you ever been diagnosed with another type of cancer?	o Yes o No
What is the name of the other cancer diagnosis you received and when (what year) did you receive this diagnosis?	
Are you currently receiving treatment for your cancer?	o Yes o No
Which treatment(s) are you CURRENTLY receiving? Please check all that apply.	☐ Chemotherapy ☐ Radiation Therapy ☐ Hormone Therapy ☐ Biological Therapy (i.e., targeted therapy) ☐ Other
If other - please indicate the treatment that you are currently receiving.	
Do you have any complications or issues related to your current treatment(s) that may interfere with your ability to complete an exercise program?	o Yes o No
Please let us know how the complication(s) or issue(s) may interfere with your ability to exercise.	
What treatment(s) have you COMPLETED for your cancer? Please check all that apply.	☐ Chemotherapy ☐ Radiation Therapy ☐ Hormone Therapy ☐ Biological Therapy (i.e., targeted therapy) ☐ Stem Cell Transplantation ☐ Surgery (vertebroplasty, orthopedic surgery, etc.) ☐ Other
If other - please indicate the treatment that you received	
When did you complete your cancer treatment(s)?	
Do you currently have any ongoing issues from your cancer and/or its treatments that may interfere with your ability to participate in an exercise program?	o Yes o No

Please let us know how this issue(s) may interfere with your ability to exercise.	
Over the past 1-2 WEEKS, what medications do you typically take to manage your pain? (This could include medications like ibuprofen, naproxen, gabapentin, opiates, etc.) Please include: - the medication name (e.g. Naproxen) - the dosage (e.g. 500 mg) - the frequency you take it (e.g. 2x/day) NOTE: if your medications or medication use changes over the course of your exercise program, please notify us of the change.	

Exercise has the potential to positively impact a number of the side effects from cancer and its treatments that are commonly experienced by people with cancer.	
Please select any of the listed side effects or issues that you are experiencing as a direct result of your cancer and/or its treatments. With this information, it may be possible for our staff to modify your exercise program to better match your specific issue(s) and potentially help you to get more out of participating in the study.	☐ Fatigue ☐ Pain ☐ Peripheral neuropathy or other nerve damage ☐ Osteoporosis or bone loss ☐ Muscle or joint issues (e.g. loss of mass, reduced range of motion, pain, stiffness) ☐ Cognitive challenges (learning or memory problems, chemo brain, brain fog) ☐ Weight maintenance issues ☐ Breathing issues ☐ Heart issues ☐ Other issue(s) or concerns that you feel exercise might specifically benefit for you
Provide more detail regarding the fatigue you indicated above, including: - severity of the fatigue - things that make your fatigue better or worse - how it might interfere with your ability to exercise	
Provide more detail regarding the pain you indicated above, including: - location in the body - cause if known - current management - how it might interfere with your ability to exercise	
Provide more detail regarding the peripheral neuropathy or nerve damage you indicated above, including: - location in the body - cause if known - current management - how it might interfere with your ability to exercise	

Provide more detail regarding the osteoporosis or bone loss you indicated above, including: - location in the body - severity of bone loss - current management - how it might interfere with your ability to exercise	
Provide more detail regarding the muscle or joint issue you indicated above, including: - location in the body - cause if known - current management - how it might interfere with your ability to exercise	
Provide more detail regarding the cognitive challenge you indicated above, including: - the specific issue you are having - current management strategies - how it might interfere with your ability to exercise	
Provide more detail regarding the breathing issue you indicated above, including: - the specific issue you are having - current management - how it might interfere with your ability to exercise	
Provide more detail regarding the heart issue you indicated above, including: - the specific issue you are having - current management - how it might interfere with your ability to exercise	
Provide more detail regarding the other issue or concern you indicated above, including: - the specific issue or concern you have - current management strategies - how it might interfere with your ability to exercise	

The following questions relate to your exercise preferences and the current set-up you have at home to complete the exercise program. Your answers will help us design a program that fits you best.	
Please check your exercise type preferences (select all that apply)	☐ Cardiovascular exercise (walking, biking, treadmill, etc.) ☐ Weight training (dumbbells, weight machines) ☐ Circuit training (bootcamp style) ☐ Group class workout ☐ Individual gym workout ☐ Other
If other, please specify:	
Please identify your fitness goals coming into the program:	☐ To build muscle ☐ To improve energy throughout the day ☐ To lose weight ☐ To get “toned” ☐ To increase strength ☐ To improve performance

	☐ To get “in shape” ☐ To be healthier ☐ To meet people ☐ To increase flexibility ☐ To improve endurance ☐ Other
If other, please specify:	
When would be the best time for you to attend a virtual exercise class?	o Morning o Afternoon o Evening o Doesn’t Matter
What kind of device do you plan to use to access the exercise app and join exercise classes?	☐ Laptop ☐ Desktop computer ☐ Cellphone ☐ Tablet ☐ other
If other, please specify	
Do you have space, in your house, where you can exercise safely while looking at your device?	o Yes o No
Do you currently have any health issues/conditions limiting your mobility or your ability to get up and down from the floor in a safe manner?	o Yes o No
If yes, please tell us more about it:	
Would someone in your household be present when you are exercising with the app?	o All the time o Sometimes o Maybe o Never
What exercise equipment do you have access to (e.g., treadmill, dumbbell weights, exercise bands, steps, etc.)?	

Appendix E: Demographic Variables

Demographic Information

Study ID: _____ Initials: _____ Date: _____

1. Date of Birth: ___ _____ _____ (DD/MM/YYYY) Age: _____
2. PHN: _____-_____ Alberta Cancer ID: _____
3. Marital Status: Never Married _____ Married _____ Common Law _____

   Separated _____ Widowed _____ Divorced_____
4. Education (check highest level attained):

   Some High School _____ Completed High School _____

   Some University/College _____ Completed University/College _____

   Some Graduate School _____ Completed Graduate School _____
5. Annual Family Income: < 20,000 _____ 20-39,999 _____ 40-59,999 _____

   60-79,999 _____ 80-99,999 _____ > 100,000 _____
6. Current Employment Status: Disability _____Retired _____ Part Time _____

   Homemaker _____ Full Time _____ Temporarily Unemployed _____
7. Location of residence/ home? _____
8. Ethnic origin or ancestry? _____ (or underline all that apply)

• British, Western European, Eastern European, French, Northern European, Southern European, Aboriginal, East and Southeast Asian, Southern Asian, Western Asian, Pacific Islands, Arab, Latin/Central and South American, Caribbean, African, Other

9. Smoking status:

   ____ Never Smoked ____ Ex-Smoker ____ Occasional Smoker

   ____ Regular Smoker (smoke every day)
10. Drinking status:

    ____ Never Drank ____ Ex-Drinker ____ Social Drinker ____ Regular Drinker (drink every day)

Appendix F: PAR-Q+

2019 PAR-Q+

The Physical Activity Readiness Questionnaire for Everyone

The health benefits of regular physical activity are clear; more people should engage in physical activity every day of the week. Participating in physical activity is very safe for MOST people. This questionnaire will tell you whether it is necessary for you to seek further advice from your doctor OR a qualified exercise professional before becoming more physically active.

GENERAL HEALTH QUESTIONS

Please read the 7 questions below carefully and answer each one honestly: check YES or NO.	YES	NO
1) Has your doctor ever said that you have a heart condition ☐ OR high blood pressure ☐?	☐	☐
2) Do you feel pain in your chest at rest, during your daily activities of living, **OR** when you do physical activity?	☐	☐
3) Do you lose balance because of dizziness **OR** have you lost consciousness in the last 12 months? Please answer **NO** if your dizziness was associated with over-breathing (including during vigorous exercise).	☐	☐
4) Have you ever been diagnosed with another chronic medical condition (other than heart disease or high blood pressure)? **PLEASE LIST CONDITION(S) HERE:**	☐	☐
5) Are you currently taking prescribed medications for a chronic medical condition? **PLEASE LIST CONDITION(S) AND MEDICATIONS HERE:**	☐	☐
6) Do you currently have (or have had within the past 12 months) a bone, joint, or soft tissue (muscle, ligament, or tendon) problem that could be made worse by becoming more physically active? Please answer **NO** if you had a problem in the past, but it **does not limit your current ability** to be physically active. **PLEASE LIST CONDITION(S) HERE:**	☐	☐
7) Has your doctor ever said that you should only do medically supervised physical activity?	☐	☐

If you answered NO to all of the questions above, you are cleared for physical activity.
Please sign the PARTICIPANT DECLARATION. You do not need to complete Pages 2 and 3.

- Start becoming much more physically active – start slowly and build up gradually.
- Follow International Physical Activity Guidelines for your age (www.who.int/dietphysicalactivity/en/).
- You may take part in a health and fitness appraisal.
- If you are over the age of 45 yr and NOT accustomed to regular vigorous to maximal effort exercise, consult a qualified exercise professional before engaging in this intensity of exercise.
- If you have any further questions, contact a qualified exercise professional.

PARTICIPANT DECLARATION
If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that the community/fitness center may retain a copy of this form for its records. In these instances, it will maintain the confidentiality of the same, complying with applicable law.

NAME _____ DATE _____

SIGNATURE _____ WITNESS _____

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER _____

If you answered YES to one or more of the questions above, COMPLETE PAGES 2 AND 3.

Delay becoming more active if:

- You have a temporary illness such as a cold or fever; it is best to wait until you feel better.
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ at **www.eparmedx.com** before becoming more physically active.
- Your health changes - answer the questions on Pages 2 and 3 of this document and/or talk to your doctor or a qualified exercise professional before continuing with any physical activity program.

11-01-2018

2019 PAR-Q+

FOLLOW-UP QUESTIONS ABOUT YOUR MEDICAL CONDITION(S)

1. Do you have Arthritis, Osteoporosis, or Back Problems?
If the above condition(s) is/are present, answer questions 1a-1c If **NO** ☐ go to question 2

1a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments) YES ☐ NO ☐

1b. Do you have joint problems causing pain, a recent fracture or fracture caused by osteoporosis or cancer, displaced vertebra (e.g., spondylolisthesis), and/or spondylolysis/pars defect (a crack in the bony ring on the back of the spinal column)? YES ☐ NO ☐

1c. Have you had steroid injections or taken steroid tablets regularly for more than 3 months? YES ☐ NO ☐

2. Do you currently have Cancer of any kind?
If the above condition(s) is/are present, answer questions 2a-2b If **NO** ☐ go to question 3

2a. Does your cancer diagnosis include any of the following types: lung/bronchogenic, multiple myeloma (cancer of plasma cells), head, and/or neck? YES ☐ NO ☐

2b. Are you currently receiving cancer therapy (such as chemotherapy or radiotherapy)? YES ☐ NO ☐

3. Do you have a Heart or Cardiovascular Condition? This includes Coronary Artery Disease, Heart Failure, Diagnosed Abnormality of Heart Rhythm
If the above condition(s) is/are present, answer questions 3a-3d If **NO** ☐ go to question 4

3a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments) YES ☐ NO ☐

3b. Do you have an irregular heart beat that requires medical management? (e.g., atrial fibrillation, premature ventricular contraction) YES ☐ NO ☐

3c. Do you have chronic heart failure? YES ☐ NO ☐

3d. Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months? YES ☐ NO ☐

4. Do you have High Blood Pressure?
If the above condition(s) is/are present, answer questions 4a-4b If **NO** ☐ go to question 5

4a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments) YES ☐ NO ☐

4b. Do you have a resting blood pressure equal to or greater than 160/90 mmHg with or without medication? (Answer **YES** if you do not know your resting blood pressure) YES ☐ NO ☐

5. Do you have any Metabolic Conditions? This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes
If the above condition(s) is/are present, answer questions 5a-5e If **NO** ☐ go to question 6

5a. Do you often have difficulty controlling your blood sugar levels with foods, medications, or other physician-prescribed therapies? YES ☐ NO ☐

5b. Do you often suffer from signs and symptoms of low blood sugar (hypoglycemia) following exercise and/or during activities of daily living? Signs of hypoglycemia may include shakiness, nervousness, unusual irritability, abnormal sweating, dizziness or light-headedness, mental confusion, difficulty speaking, weakness, or sleepiness. YES ☐ NO ☐

5c. Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, **OR** the sensation in your toes and feet? YES ☐ NO ☐

5d. Do you have other metabolic conditions (such as current pregnancy-related diabetes, chronic kidney disease, or liver problems)? YES ☐ NO ☐

5e. Are you planning to engage in what for you is unusually high (or vigorous) intensity exercise in the near future? YES ☐ NO ☐

11-01-2018

2019 PAR-Q+

6. Do you have any Mental Health Problems or Learning Difficulties? This includes Alzheimer's, Dementia, Depression, Anxiety Disorder, Eating Disorder, Psychotic Disorder, Intellectual Disability, Down Syndrome
If the above condition(s) is/are present, answer questions 6a-6b If **NO** ☐ go to question 7

6a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments) YES ☐ NO ☐

6b. Do you have Down Syndrome **AND** back problems affecting nerves or muscles? YES ☐ NO ☐

7. Do you have a Respiratory Disease? This includes Chronic Obstructive Pulmonary Disease, Asthma, Pulmonary High Blood Pressure
If the above condition(s) is/are present, answer questions 7a-7d If **NO** ☐ go to question 8

7a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments) YES ☐ NO ☐

7b. Has your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require supplemental oxygen therapy? YES ☐ NO ☐

7c. If asthmatic, do you currently have symptoms of chest tightness, wheezing, laboured breathing, consistent cough (more than 2 days/week), or have you used your rescue medication more than twice in the last week? YES ☐ NO ☐

7d. Has your doctor ever said you have high blood pressure in the blood vessels of your lungs? YES ☐ NO ☐

8. Do you have a Spinal Cord Injury? This includes Tetraplegia and Paraplegia
If the above condition(s) is/are present, answer questions 8a-8c If **NO** ☐ go to question 9

8a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments) YES ☐ NO ☐

8b. Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting? YES ☐ NO ☐

8c. Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)? YES ☐ NO ☐

9. Have you had a Stroke? This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event
If the above condition(s) is/are present, answer questions 9a-9c If **NO** ☐ go to question 10

9a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments) YES ☐ NO ☐

9b. Do you have any impairment in walking or mobility? YES ☐ NO ☐

9c. Have you experienced a stroke or impairment in nerves or muscles in the past 6 months? YES ☐ NO ☐

10. Do you have any other medical condition not listed above or do you have two or more medical conditions?
If you have other medical conditions, answer questions 10a-10c If **NO** ☐ read the Page 4 recommendations

10a. Have you experienced a blackout, fainted, or lost consciousness as a result of a head injury within the last 12 months **OR** have you had a diagnosed concussion within the last 12 months? YES ☐ NO ☐

10b. Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)? YES ☐ NO ☐

10c. Do you currently live with two or more medical conditions? YES ☐ NO ☐

PLEASE LIST YOUR MEDICAL CONDITION(S) AND ANY RELATED MEDICATIONS HERE:

GO to Page 4 for recommendations about your current medical condition(s) and sign the PARTICIPANT DECLARATION.

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2019 PAR-Q+

If you answered NO to all of the FOLLOW-UP questions (pgs. 2-3) about your medical condition, you are ready to become more physically active – sign the PARTICIPANT DECLARATION below:

- It is advised that you consult a qualified exercise professional to help you develop a safe and effective physical activity plan to meet your health needs.
- You are encouraged to start slowly and build up gradually - 20 to 60 minutes of low to moderate intensity exercise, 3-5 days per week including aerobic and muscle strengthening exercises.
- As you progress, you should aim to accumulate 150 minutes or more of moderate intensity physical activity per week.
- If you are over the age of 45 yr and **NOT** accustomed to regular vigorous to maximal effort exercise, consult a qualified exercise professional before engaging in this intensity of exercise.

If you answered **YES** to **one or more of the follow-up questions** about your medical condition:
You should seek further information before becoming more physically active or engaging in a fitness appraisal. You should complete the specially designed online screening and exercise recommendations program - the **ePARmed-X+ at www.eparmedx.com** and/or visit a qualified exercise professional to work through the ePARmed-X+ and for further information.

Delay becoming more active if:

- You have a temporary illness such as a cold or fever; it is best to wait until you feel better.
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ **at www.eparmedx.com** before becoming more physically active.
- Your health changes - talk to your doctor or qualified exercise professional before continuing with any physical activity program.

- You are encouraged to photocopy the PAR-Q+. You must use the entire questionnaire and NO changes are permitted.
- The authors, the PAR-Q+ Collaboration, partner organizations, and their agents assume no liability for persons who undertake physical activity and/or make use of the PAR-Q+ or ePARmed-X+. If in doubt after completing the questionnaire, consult your doctor prior to physical activity.

PARTICIPANT DECLARATION

- All persons who have completed the PAR-Q+ please read and sign the declaration below.
- If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that the community/fitness center may retain a copy of this form for records. In these instances, it will maintain the confidentiality of the same, complying with applicable law.

NAME _____ DATE _____

SIGNATURE _____ WITNESS _____

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER _____

For more information, please contact
www.eparmedx.com
Email: eparmedx@gmail.com

Citation for PAR-Q+
Warburton DER, Jamnik VK, Bredin SSD, and Gledhill N on behalf of the PAR-Q+ Collaboration. The Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) and Electronic Physical Activity Readiness Medical Examination (ePARmed-X+). Health & Fitness Journal of Canada 4(2):3-23, 2011.

The PAR-Q+ was created using the evidence-based AGREE process (1) by the PAR-Q+ Collaboration chaired by Dr. Darren E. R. Warburton with Dr. Norman Gledhill, Dr. Veronica Jamnik, and Dr. Donald C. McKenzie (2). Production of this document has been made possible through financial contributions from the Public Health Agency of Canada and the BC Ministry of Health Services. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada or the BC Ministry of Health Services.

Key References
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3. Chisholm DM, Collis ML, Kulak LL, Davenport W, and Gruber N. Physical activity readiness. British Columbia Medical Journal. 1975;17:375-378.
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11-01-2018

Appendix G: Medical Variables

Study ID: _____ Initials: _____ Date: _____

1. Date of initial diagnosis of cancer: _____ (DD/MM/YYYY)
2. Type of cancer: _____

Histopathological details: _____

Bone involvement? ____

If so, where? _____

Staging:

- ISS stage: _____
- CA by iFISH: _____
- LDH: _____
- Overall stage: _____

TREATMENT DETAILS:

3. **Systemic Therapy: _____**

a. Name: _____ Cycles; _____
   Dates: _____

b. Name: _____ Cycles; _____
   Dates: _____

c. Name: _____ Cycles; _____
   Dates: _____

d. Name: _____ Cycles; _____
   Dates: _____

e. Name: _____ Cycles; _____
   Dates: _____

4. **Surgery: yes____ no____**

a. Location of
   surgery:_____

b. Details of surgery:

_____

5. **Radiation Therapy**: **yes____ no____**

a. Location_____

b. Dosage: _____ Fractions: _____Dates: _____

MEDICAL HISTORY:

6. Relevant past medical history: _____

7. Co-morbid/ concurrent conditions: _____

_____

8. Medications:

Medication	**Reason**	**Dosage/Frequency**	**Date Started**

Appendix H: Health-Related Quality of Life Measures

FACT-G

FACT-G (Version 4)

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

	PHYSICAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box ☐ and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

FACT-G (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	EMOTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

FACIT-F

FACIT-F (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
HI7	I feel fatigued	0	1	2	3	4
HI12	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble starting things because I am tired	0	1	2	3	4
An4	I have trouble finishing things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
An16	I have to limit my social activity because I am tired	0	1	2	3	4

FACT-MM

FACT-MM (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
P2	I have certain parts of my body where I experience pain	0	1	2	3	4
HI 12	I feel weak all over	0	1	2	3	4
BMT 6	I get tired easily	0	1	2	3	4
HI8	I have trouble concentrating	0	1	2	3	4
N3	I worry about getting infections	0	1	2	3	4
LEU 3	I feel discouraged about my illness	0	1	2	3	4
LEU 4	Because of my illness, I have difficulty planning for the future	0	1	2	3	4
LEU 6	I worry that I might get new symptoms of my illness	0	1	2	3	4
BRM 9	I have emotional ups and downs	0	1	2	3	4
BP1	I have bone pain	0	1	2	3	4
An 14	I need help doing my usual activities	0	1	2	3	4
MM 1	I have trouble walking because of pain	0	1	2	3	4
HI7	I feel fatigued	0	1	2	3	4
ES 10	I have gained weight	0	1	2	3	4

FACT-BP

FACT-BP
QUALITY OF LIFE MEASUREMENT IN PATIENTS WITH BONE PAIN

Please answer the following questions about your bone pain. Sometimes it is not easy to tell whether a pain you might have is bone pain or some other type of pain. Please do the best you can to answer these questions about your bone pain in particular. Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

Q7	In how many places in your body have you felt bone pain?	0	1	2	3	4+

		Not at all	A little bit	Some-what	Quite a bit	Very much
GF7	I am content with the quality of my life right now	0	1	2	3	4
P2	I have certain parts of my body where I experience pain	0	1	2	3	4
BP1	I have bone pain	0	1	2	3	4
BP2	It hurts when I put weight or pressure on the place where I have bone pain	0	1	2	3	4
BP3	I have bone pain even when I sit or lie still	0	1	2	3	4
BP4	I need help doing my usual activities because of bone pain	0	1	2	3	4
BP5	I am forced to rest during the day because of bone pain	0	1	2	3	4
BP6	I have trouble walking because of bone pain	0	1	2	3	4
BP7	Bone pain interferes with my ability to care for myself (bathing, dressing, eating, etc.)	0	1	2	3	4
BP8	Bone pain interferes with my social activities	0	1	2	3	4
BP9	Bone pain wakes me up at night	0	1	2	3	4
BP 10	I am frustrated by my bone pain	0	1	2	3	4
BP 11	I feel depressed about my bone pain	0	1	2	3	4
BP 12	I worry that my bone pain will get worse	0	1	2	3	4
BP 13	My family has trouble understanding when my bone pain interferes with my activity	0	1	2	3	4

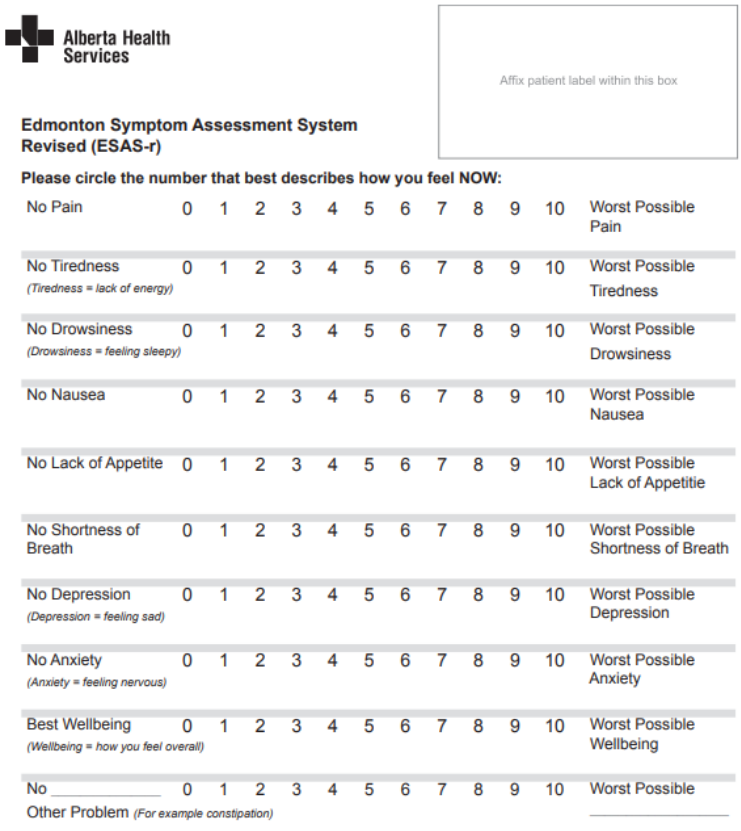
FACT/GOG-NTX-4

FACT/GOG-NTX-4 (Version 4)

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

		Not at all	A little bit	Some-what	Quite a bit	Very much
NTX 1	I have numbness or tingling in my hands	0	1	2	3	4
NTX 2	I have numbness or tingling in my feet	0	1	2	3	4
NTX 3	I feel discomfort in my hands	0	1	2	3	4
NTX 4	I feel discomfort in my feet	0	1	2	3	4

Appendix I: Edmonton Symptom Assessment Scale and the Canadian Problem Checklist



Alberta Health Services

Affix patient label within this box

Edmonton Symptom Assessment System Revised (ESAS-r)

Please circle the number that best describes how you feel NOW:

No Pain	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Pain
No Tiredness *(Tiredness = lack of energy)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Tiredness
No Drowsiness *(Drowsiness = feeling sleepy)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Drowsiness
No Nausea	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Nausea
No Lack of Appetite	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Lack of Appetitie
No Shortness of Breath	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Shortness of Breath
No Depression *(Depression = feeling sad)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Depression
No Anxiety *(Anxiety = feeling nervous)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Anxiety
Best Wellbeing *(Wellbeing = how you feel overall)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Wellbeing
No _____ Other Problem *(For example constipation)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible _____

Screening for Distress
(Canadian Problem Checklist)

Please check all of the following items that have been a CONCERN or PROBLEM for you in the past week, including today:

Practical:	☐ Work/School ☐ Finances ☐ Getting to and from appointments ☐ Accommodations ☐ Medication Coverage
Social/Family:	☐ Feeling a burden to others ☐ Worry about friends/family ☐ Feeling Alone ☐ Relationship difficulties
Emotional:	☐ Fears/Worries ☐ Sadness ☐ Frustration/Anger ☐ Changes in Appearance ☐ Intimacy/Sexuality
Spiritual:	☐ Meaning/Purpose of Life ☐ Faith
Informational:	☐ Understanding my illness and/or treatment ☐ Talking with the health care team ☐ Making treatment decisions ☐ Knowing about available resources
Physical:	☐ Concentration/memory ☐ Sleep ☐ Weight ☐ Swallowing

	0	1	2	3	4	5	6	7	8	9	10
Please indicate the number (0-10) that best describes how much distress you have been experiencing in the past week, including today: (0-No distress and 10-Worst possible distress) * must provide value	○	○	○	○	○	○	○	○	○	○	○

Appendix J: Satisfaction Survey

Satisfaction Survey

How did you find out about the study/program?

- ◯ A physician or a nurse at my cancer hospital
- ◯ A staff member in the rehab department at my cancer hospital
- ◯ The Myeloma Alberta Support Society
- ◯ As a former participant in the Alberta Cancer Exercise (ACE) program
- ◯ Other

If other, please specify: _____

Please answer the following questions regarding the exercise program and the staff. Please select the answer that best describe how you feel.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
Completing the exercise program helped me meet my health and wellness goals	◯	◯	◯	◯	◯
The exercise program helped me manage symptoms and side effects related to my cancer and/or treatments	◯	◯	◯	◯	◯
The exercise program helped me increase my knowledge related to the benefits of physical activities for cancer survivors	◯	◯	◯	◯	◯
The program staff made me feel comfortable	◯	◯	◯	◯	◯
The program staff were knowledgeable	◯	◯	◯	◯	◯
The program staff were informative and made an effort to teach me about my health and wellness	◯	◯	◯	◯	◯
The program staff helped me meet my health and wellness goals	◯	◯	◯	◯	◯
The program staff seemed to care about my personal health and wellbeing	◯	◯	◯	◯	◯
The program staff were supportive	◯	◯	◯	◯	◯
The program staff worked with me to ensure the exercises were appropriate for my level of fitness and my symptoms	◯	◯	◯	◯	◯

Overall, the service you received from the program staff was:

- ◯ Poor
- ◯ Below average
- ◯ Average
- ◯ Above average
- ◯ Excellent

The following questionnaire asks you how you feel about the MY PROGRESS program. Please read each question carefully and select the answer that best represents your feeling.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
How beneficial was the exercise program?	○	○	○	○	○
How enjoyable was the exercise program?	○	○	○	○	○
How supportive were your family/friends of the exercise program?	○	○	○	○	○
How motivated were you to do the exercise program?	○	○	○	○	○
How difficult was it for you to do the exercise program?	○	○	○	○	○

Now that you have completed the 12-week exercise program, the following questions ask about your plans to continue exercising in the next year.

Please select the answer that best represents how you feel.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
How beneficial do you think it will be for you to continue exercising?	○	○	○	○	○
How enjoyable do you think it will be for you to continue exercising?	○	○	○	○	○
How supportive do you think your family/friends will be if you try to continue exercising?	○	○	○	○	○
How motivated are you to continue to exercise?	○	○	○	○	○
How difficult do you think it will be for you to continue exercising?	○	○	○	○	○
How confident are you to continue exercising on your own?	○	○	○	○	○
Do you feel that the MY PROGRESS program prepared you to exercise on your own?	○	○	○	○	○

How much of a burden was it for you to complete each of the following:

	Not at all	A little bit	Somewhat	Quite a bit	Very much
The 2 minute step test	○	○	○	○	○
The muscular strength, balance, and flexibility testing	○	○	○	○	○
The online questionnaires	○	○	○	○	○
The independent exercise sessions	○	○	○	○	○
The live exercise sessions	○	○	○	○	○
Learning how to use the application (Heal-Me)	○	○	○	○	○
Using the application (Heal-Me) to exercise	○	○	○	○	○

Looking back, how do you feel about your participation in the exercise program?					
	Not at all	A little bit	Somewhat	Quite a bit	Very much
It was rewarding	○	○	○	○	○
It was a waste of my time	○	○	○	○	○
It will be useful for research helping others	○	○	○	○	○
It was useful for me personally	○	○	○	○	○
I would recommend the exercise program to other cancer patients	○	○	○	○	○

Please provide us with any additional information regarding MY PROGRESS or the Heal-Me application that you feel is important for us to know, but was not covered in the questions above.
(e.g. additional strengths or weaknesses of the program, specific benefits or negative aspects that you experienced, etc.)

_____

Would you like to be contacted if and when our research group has future research studies or programs that you would be eligible for?

○ Yes
○ No

Appendix K: Virtual Physical Assessment Protocols

DETAILED PROTOCOLS FOR FITNESS ASSESSMENTS

1) Resting Vital Measurements

NOTE: Discuss with participant even if not measuring to see if recent values and/or any related issues are known.

a) Resting Heart Rate

- If participant has device at home, have them provide the value (bpm) after they are seated for 5 minutes.
- **If a heart rate monitor is NOT available**, attempt to instruct the participant through the following steps to obtain a resting heart rate measurement:
  - Participant will require a stopwatch, or tester can show time on screen if possible.
  - After 5 minutes, ask the participant to use their index and middle finger to apply gentle pressure at the wrist proximal to the thumb.
  - Use a 15-second count to determine the resting heart rate. Start the measurement time period simultaneously with counting the first beat as "0".
  - Multiply the participant's count by 4 and record the measurement in beats per minute (bpm).
- If the heart rate is measured at ≥100 bpm, wait 5 minutes (participant should sit quietly during this time) and take the measurement again.
- If the resting heart rate is still ≥100 bpm, DO NOT allow the participant to continue with the musculoskeletal or aerobic fitness components of the assessment.

b) Resting Blood Pressure (*OPTIONAL*)

- If participant has a blood pressure monitor and this measure is deemed relevant, this can be taken immediately after the resting heart rate measurement (or at the same time as heart rate depending on the device), while the participant is still seated.
- Ask the participant to place the cuff of their blood pressure monitor on their upper left arm (or right if necessary – i.e. surgery on left side).
  - Correct cuff or arm position if necessary, prior to the measurement.
  - Ask them to rest their arm and sit quietly during the measurement.
- Have the participant provide the value measure by the monitor.
  - If the resting systolic blood pressure is >144 mmHg and/or if the resting diastolic blood pressure is >94 mmHg, wait 5 minutes (participant should sit quietly during this time) and take the measurement again.

- If the resting systolic blood pressure is >144 mmHg or if the resting diastolic blood pressure is >94 after the second reading, DO NOT have the participant attempt the musculoskeletal or aerobic fitness components of the assessment.

c) Resting Oxygen Saturation (SpO_2) Measurement (*OPTIONAL*)

- This measurement will ONLY be taken where a pulse oximeter is available and is deemed relevant.
- Take measurement immediately after the other resting measurements, while the participant is still seated.
- Ask them to place the oximeter on their index or ring finger and rest their arm while sitting quietly during the measurement.
- Ask the participant to provide the value after a stable measurement is obtained.
- Record the % oxygen saturation (SpO_2).

2) Body Composition

a) Weight

- Ask the participant to self-report the most recent measure of their weight, or if the participant has a home scale this value for can be used instead provided:
  - The participant took the measurement with no shoes, heavy jewelry or items in pockets, or any unnecessary clothing (e.g. Sweatshirt).
  - The scale was resting on a hard, flat surface, and correctly zeroed.
  - Use same scale for any follow-up measures.
- The measurement can be taken prior to testing or off-camera during testing session if more efficient and/or scale cannot be moved.
- Record weight as precise as possible to the nearest 0.1 kg if possible. Convert from pounds if necessary.

b) Standing Height

- Ask the participant to self-report the most recent measure of their height.
- Record the height provided in cm (convert from inches if necessary).

3) Aerobic Fitness Measurement

2 Minute Step Test

- Explain to the participant that you will now test their aerobic fitness with a step test.
- Set-up:
  - Have the participant measure midway between the patella (kneecap) and iliac

crest (top of the hip bone), which will be the required height for the test.
    - If possible, place a corresponding mark (e.g. piece of tape) on the wall and record this height on the data sheet.
    - Have the participant stand perpendicular to the camera, where you can also observe the knee reaching the required height on the wall.
- Prior to starting, instruct the participant to slow down or rest if they become too tired.
    - If the participant requires a break during the test, instruct them to take a seat but the 2-minute time period will continue as they rest, and they can continue once they are feeling recovered if time allows. Record the number of and reason for any breaks.
- Ask the participant to inform you at any point during the test if they feel dizzy, lightheaded, nauseous, or heaviness, tightness or constricting in the chest, down the arm or into the shoulders or upper back.
- Test:
    - The participant will complete as many alternating steps as they can by lifting the knees to the indicated height as they can in the 2 minutes.
        - Test should be done as a march, where one foot is always in contact with the ground.
        - Only count steps that the marked height is reached by the RIGHT knee.
            - Provide one warning regarding height (do not count step).
            - If participant does not reach height on 2 consecutive steps, have them slow to a pace where they can reach it or rest until they recover where the height can be reached again.
    - Inform the participant that you will give them a 'ready-set- go' cue to start the test by lifting the RIGHT leg first. Ensure that you start your stopwatch simultaneously with 'go'.
- Once the 2 minutes is complete, have them cool down by walking lightly on the spot for one minute afterwards.
- Record the number of times the RIGHT knee reaches the required height.
- Ask the participant for a Rating of Perceived Exertion (Borg Scale 0–10) at the end.
- If deemed necessary (and possible), have the participant sit down provide a recovery HR / BP / SpO2 measurement 3 to 5 minutes post-test (following resting vitals protocols).

4) Flexibility

a) Active Shoulder Flexion

- Explain to the participant that you will now assess their shoulder flexibility.

- Have the participant sit (without their back touching the chair) with their arms by their sides and palms facing the body.
    - The chair will need to be perpendicular to camera with movement in full view of the camera. Chair will need to be rotated 180 degrees for opposite arm.
- Instruct the participant to lead with the thumb and attempt to raise their arm in an arc out in front and then above the body while remaining in the sagittal plane, aiming to bring their hand above their shoulder and as far back as possible.
    - Instruct them to not arch their back, bend the elbow, or move out of the sagittal plane (will be difficult to see given position set up to camera).
    - Remind the participant to only move within a pain-free range of motion.
- Have the participant hold the final position, take a screen shot as quickly as possible.
- Take the measurement a second time on the same arm, then have the participant rotate the chair and completed the measurement twice on the other arm.
- Determine the measurements in degrees using a goniometer over the screenshots.

b) <u>Sit and Reach</u>

OPTIONAL: Completing this test will require both something to measure (ruler, measuring tape) and another person for determining the distance reached.

- Explain to the participant that you will now test the flexibility of their hamstrings and low-back.
- Ask the participant to remove their footwear and move their chair against a wall if possible to prevent it from moving during the test.
- Ask the participant to sit on the edge of a chair and have them warm-up by stretching their hamstrings in a similar movement to the test below.
- Now, instruct the participant to extend one leg forward with the knee straight, heel on the floor, and ankle bent at 90° (ankle should stay at same angle during test).
    - For the other leg, the knee should be bent and foot flat on the ground
- Instruct the participant to extend their arms fully with one hand on top of the other, both palms facing down, and tips of middle fingers evenly lined up.
- Next, ask the participant to exhale while slowly reaching forward moving their hands as far as they can toward the toes, keeping their back straight without bending their knee or changing the angle in their ankle.
    - Tell the participant the movement should be slow and controlled, and to avoiding bouncing or quick movements.
- Ask the participant to hold the position of maximum flexion long enough for the measurement to be taken.

- Complete two trials per leg and record each measurement to the nearest 0.5cm.
- If the participant does not reach past the toe(s), measure the distance from the toes to fingertip and record this as a negative score; at the toes = 0 cm; positive score beyond the toes.

5) Musculoskeletal Fitness Measurements

a) <u>Sit to Stand Test</u>

- Explain to the participant they will now be doing a sit to stand test to assess the muscular strength & endurance of their legs.
- If possible, the chair should:
  - Be close to 17" (43 cm) in height.
    - Have participant measure where possible and record the height.
    - Use same chair for any follow-up testing. Record details (color, etc.)
  - Not be cushioned or have arms.
  - Be placed against a wall to prevent the chair from moving during the test.
  - Be set-up perpendicular to the camera so tester can view entire movement from the side.
- Have the participant start in the seated position with arms crossed at their chest. Their back should be straight and not touching the back of the chair.
- They will rise to a full stand and then return to the fully seated starting position.
  - They must stand with full hip extension and return to the seated position with their bottom in contact with the chair for the repetition to count.
- Ask the participant to complete as many repetitions as they can in 30 seconds, moving as fast as possible while maintaining balance and control of the movement.
- Inform the participant that you will give them a 'ready-set- go' cue to start the test.
  - Ensure that you start your stopwatch simultaneously with 'go'.
- Record the full number of stands completed in the 30 seconds.

b) <u>One-Leg Stance Test (Balance)</u>

- Explain to the participant that you will now test their balance.
- The participant should complete the test on a flat and stable surface, and be near a stable object (wall, counter, table…) for safety in case of loss of balance.
- Instruct them to stand with legs shoulder width apart with arms crossed against the chest, hands on opposite shoulders (or both hands on hips).
  - Have the participant facing directly toward the camera.
- Recommend that they should focus on a point at eye-level in front of them during the trials.

- Client stands on leg of choice, lifting the other foot so it is near the ankle of the other foot.
    - Make sure foot is not touching or resting on the opposite leg or foot, and there is some space between the legs.
- Time starts as soon as the participant is in the above position.
- Hold for as long as possible to a limit of 45 seconds.
- The **test stops** when:
    - Arms move away from the body.
    - The raised foot moves toward or away from the standing limb or touches the floor.
    - The weight bearing foot moves.
    - 45 seconds is reached.
- Repeat the test on the opposite leg and record the score for each leg.
- If the participant loses balance in the first 3 seconds of a trial, they are allowed a second trial on the same leg.

c) <u>Plank Test</u>

- Explain to the participant they will be doing a plank test to assess their core muscular endurance.
- Have the participant start lying prone on a mat on the floor.
    - Their body should be perpendicular to the camera view, so position of entire body can be observed.
- Instruct the participant to lift off of the floor mat and hold the following position as long as possible WITHOUT PAIN:
    - Resting on forearms and feet dorsiflexed with weight on the balls of the toes.
    - Elbows should be beneath the shoulders, and arms can be separated or with fingers linked.
    - Hips in line with the trunk – NOT above or sagging below.
    - Feet together and legs (knees) must be straight.
    - Participant should look straight down (head & neck in neutral position).
    - Tell the participant to not hold their breath while completing the test.
- Begin timing the test when the participant has taken the correct starting position.
- Stop & record the time (to the nearest second) when they can no longer maintain proper form (body lowers or rises out of starting position) OR they return to the floor/mat.

Appendix L: Workout Example

*modifications provided in all cases, as needed

Warm-Up

Exercise	**Duration**	**Cumulative Time (mm:ss)**
Shadow Boxing Combo 1	60s	1:00
Shadow Boxing Combo 2	60s	2:00
Transition	*30s*	2:30
Standing March	45s	3:15
Standing March with Lateral Raise	45s	4:00
Transition	*30s*	4:30
Step Touch	45s	5:15
Step Touch with Jab	45s	6:00
Transition	*30s*	6:30
Squat Calf Raise	45s	7:15
Butt Kick	45s	8:00
Butt Kick with High Row	45s	8:45
Transition	*15s*	9:00
High Knee March	30s	9:30
High Knee with Pulldown	30s	10:00

Main Circuit

2 Rounds - 60 seconds work, 30 seconds rest. 90 second breaks between rounds.

Exercise #	Type	Level 1 Option	Level 2 Option
1	Cardio	High Knee Tap	High Knee Tap with Resistance
2	Upper Body	YTW with Hip Hinge	Prone YTW
3	Lower Body	Inline Lunge	Reverse Lunge
4	Balance	Standing Balance with Knee Raises	One Foot Alphabet
5	Cardio	Kickbox Punch/Knee Drive Combo w/o Weights	Kickbox Punch/Knee Drive Combo with Weights
6	Upper Body	Seated Chest Press	Supine Chest Press
7	Lower Body	Sit-to-Stand	Sit-to-Stand Overhead Press
8	Core	Bird Dog (Legs Only)	Bird Dog (Full)

Additional Core

2 Rounds – 60 seconds work, 30 seconds rest. 45 second breaks between rounds.

Exercise #	Level 1 Option	Level 2 Option
1	Modified Plank (Against Wall or on Knees)	Plank
2	Glute Bridge	Glute Bridge with Leg Lift

Stretching

Stretch	**Duration/Reps**
Seated Glute Stretch	30s hold per side
Standing Hamstring Stretch	30s hold per side
Standing Quadriceps Stretch	30s hold per side
Standing Calf Stretch	30s hold per side
Shoulder Complex Stretch	30s hold per side
Pectoralis Major/Minor Stretch	30s hold per side
Low Neck & Upper Back Stretch	30s hold per side
Shoulder Rolls	10 repetition forwards, 10 repetitions backwards

Appendix M: MY PROGRESS Exercise Progression Formula

Resistance Exercise Progression Formula

Week	Independent Exercise			Group/Supervised Exercise		
---	Frequency (#)	Duration (mins)	Intensity (RPE)	Frequency (#)	Duration (mins)	Intensity (RPE)
1	1	45	3	1	60	3
2	1	45	3	1	60	3
3	1	45	3	1	60	3
4	1	45	4	1	60	4
5	1	45	4	1	60	4
6	1	45	4	1	60	4
7	2	45	4	1	60	4
8	2	45	4	1	60	4
9	2	45	4	1	60	4
10	2	45	5	1	60	5
11	2	45	5	1	60	5
12	2	45	5	1	60	5

Aerobic Progression Formula

Track A: < 90 minutes/week of moderate intensity aerobic exercise at baseline.

Week	Volume (mins)	Intensity (RPE)
1	40	3
2	50	3
3	50	3
4	50	3
5	60	3
6	60	4
7	70	4
8	70	4
9	80	4
10	80	4
11	90	4
12	90	4

Track B: ~ 90 minutes/week of moderate intensity aerobic exercise at baseline & participant's goal is to maintain current aerobic exercise while increasing resistance exercise.

Week	Volume (mins)	Intensity (RPE)
1	90	3
2	90	3
3	90	3
4	90	3
5	90	3
6	90	3
7	90	4
8	90	4
9	90	4
10	90	4
11	90	4
12	90	4

Track C: ~ 90 minutes/week of moderate intensity aerobic exercise at baseline & participant's goal is to reach ~150 minutes/week by study completion

Week	Volume (mins)	Intensity (RPE)
1	90	3
2	100	3
3	100	3
4	110	3
5	110	3
6	120	3
7	120	4
8	130	4
9	130	4
10	140	4
11	140	4
12	150	4

Track D: ~ 150 minutes/week of moderate intensity aerobic exercise at baseline & participant's goal is to maintain current aerobic exercise while increasing resistance exercise.

Week	Volume (mins)	Intensity (RPE)
1	150	3
2	150	3
3	150	3
4	150	3
5	150	3
6	150	3
7	150	4
8	150	4
9	150	4
10	150	4
11	150	4
12	150	4