

EXERCISE TO REVERSE FRAILTY IN OLDER FEMALES

by

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B. KIN., Acadia University, 2015

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A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE OF
MASTER OF SCIENCE

in

THE COLLEGE OF GRADUATE STUDIES

(Interdisciplinary Studies)

THE UNIVERSITY OF BRITISH COLUMBIA

(Okanagan)

August 2017

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Examination Committee Form

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Abstract

The risk of becoming frail increases with age. One million Canadians are frail, placing them at greater risk for disease and disability. Frailty is easily observed yet difficult to define. No gold-standard definition exists, but most clinicians support frailty as a medical syndrome characterized as a state of mild to severe vulnerability. Sex-differences complicate frailty; females experience this syndrome sooner yet paradoxically live longer than males. Exercise might be an effective therapy for frailty; however, which components are most effective is yet unknown. This study hypothesized: 1) More individuals in an exercise (EX) intervention would reverse frailty, versus a control (CON) group; and 2) Changes in frailty would be related to improvement in functional task performance and measures of strength.

Female participants 65-81 years of age, classified as pre-frail as determined by a score of; 1-2 on the Cardiovascular Health Study-Frailty Phenotype (FP) tool or 4-6 on the Clinical Frailty Scale (CFS) or a normal gait speed (GS) between 1.0-1.5 m/sec. The EX group (n = 9) completed a 12-week exercise intervention (3 days/week, 60 min/session). Exercise included multi-component training (MCT), inclusive of aerobic, flexibility, resistance and balance training, with a focus on the latter two modalities. The CON group (n = 11) maintained their normal daily routine.

According to the FP, CFS and GS, 25, 37.5 and 62.5% more EX group participants reversed frailty status than the CON group, respectively. There was a statistically significant improvement in GS (0.24 m/sec), grip strength (3.9 kg) and sit-to-stand (STS) time (5.0 sec) within the EX group from baseline to follow-up. STS was faster in the CON group at baseline but no significant between-group difference existed at follow-up. There was also a statistically significant improvement in knee extension isometric torque (7.4 Nm) and isotonic velocity (37.5 %/sec) within the EX group

from baseline to follow-up. Elbow flexion isotonic velocity was faster (40.8 °/sec) in the EX group at follow-up but no significant between-group difference existed at baseline.

A MCT intervention that utilizes progressive resistance and balance exercise may be safe and effective at reversing frailty in pre-frail females.

Preface

This research was conducted through the Healthy Exercise and Aging Laboratory (HEAL) group at the Okanagan campus of the University of British Columbia by Dr. Gareth R. Jones, Dr. Jennifer M. Jakobi and Nicholas W. Bray. Students who assisted with the exercise program implementation and data collection for this research included Rowan Smart, Samantha Kuzyk, Cydney Richardson, Andrey Fedorov, Mathew Littlewood, Bret Yungen, Anup Dhaliwal, Savannah Frederick and Paul Cotton. Dr. Jones and Dr. Jakobi oversaw the conceptual design of the study, writing process, technical aspects of the equipment, acquisition of exercise equipment, and funding for the study. Nicholas Bray designed the study concept and experimental methodology, undertook participant recruitment, data collection and analysis, and writing of the thesis. The University of British Columbia's Clinical Research Ethics Board granted ethics approval for H16-00712 on November 3, 2016. This research is currently unpublished.

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List of Abbreviations

BMI = Body Mass Index

CFS = Clinical Frailty Scale

CI = Confidence Interval

CGA = Comprehensive Geriatric Assessment

CON = Control

cm = Centimeters

EF = Elbow Flexion

EHI = Edinburgh Handedness Inventory

EX = Exercise

FP = Frailty Phenotype

GS = Gait Speed

kg = Kilograms

KE = Knee Extension

kg/m² = Kilograms per Meter Squared

lbs = Pounds

m = Meters

MCI = Mild Cognitive Impairment

MCT = Multi-Component Training

min = Minutes

MLTPAQ = Minnesota Leisure Time Physical Activity Questionnaire

MoCA = Montreal Cognitive Assessment

m/sec = Meters Per Second

Nm = Newton Meters

OMNI-RES = OMNI – Resistance Exercise Scale

PAR-Q+ = Physical Activity Readiness – Questionnaire Plus

ROM = Range of Motion

RPE = Rating of Perceived Exertion

SPPB = Short Physical Performance Battery

SPSS = Statistical Package for the Social Sciences

STS = Sit-to-Stand

sec = Seconds

°/sec = Degrees per Second

° = Degrees

" = inches

% = Percent

Acknowledgements

First and foremost, I would like to offer my sincere thanks and gratitude to my supervisors, Dr. Gareth Jones and Dr. Jennifer Jakobi. Thank you for your patience, wisdom, support and helping me grow both as a researcher and as a person. I will be forever grateful for the experience you have provided. I would like to thank the members of my committee, Dr. Kathy Rush and Dr. Charlotte Jones for their time and advice.

I would like to acknowledge the funding provided by the UBC Okanagan Graduate Fellowship. Thank you to Clint Pratch of Flaman Fitness™ for generously donating the exercise equipment that made this study possible. Thank you to the Okanagan Men's Shed club for building the boxes that were vital to the progression of the participant's exercises.

Thank you to all those in the lab who have helped in the formation of this project. Rowan, thanks for always offering to help and being able to fix almost any problem that arose. Thanks to Andrey and Sam for not taking life too serious, for always being available to chat and provide help. Thanks to Anup, Brett, Savannah and Paul for helping run the exercise program, collect and analyze data. A special thank you to Matt, who ran the exercise program when I was unavailable and to Cydney, for allowing me to monopolize her time over the Christmas break so that we could begin the exercise program in the new year.

To all my participants, thank you for your time and dedication. This study could not have happened if it was not for you. Thank you for trusting me and allowing me to push you to limits that you did not think you could achieve. I may have been the one teaching but I learned from each one of you during our time together.

Thank you to my family for always supporting me. Thank you to my mother for her kindness, love and reminding me that *“I’ll be fine.”* Thank you to my father for teaching me an invaluable life lesson from a very young age, the value of a strong work ethic. Thank you to my brother, Scott who may be younger but inspires me to be great.

Finally, but most importantly, thank you to my fiancé, Jill. No words could ever truly describe how grateful I am for your unconditional love and support. To thank you for sticking by me during the completion of this degree would be short sighted. You have been here since the beginning of my pursuit of higher education, even when I did not know where exactly that route would take me. Regardless, you somehow recognized that I was capable of more. I would not be where I am if it was not for your love; you bring out the best in me, I love you.

To my fiancé, Jill and my family.

Chapter 1: Introduction

1.1. Epidemiology of Aging Canada

In 2015, older adults (those aged 65 years and older) outnumbered children aged 0 to 14 years. One in six Canadians (16.1 percent; %) are over the age of 65 years. Furthermore, the growth rate of the aging population is approximately four times that of the total population (Statistics Canada, 2015). An aging population is recognized as a global phenomenon (Cesari et al., 2015). The aging demographic has more females than males and this heterogeneity becomes greater with increasing age (Statistics Canada, 2016a). Across age groups, there are approximately 4.9% more females than males 65-69 years, 18.5% more females 75-79 years, and 145.5% more females 90 years of age and above (Statistics Canada, 2016a). Although female life expectancy is, on average, four years longer than that of males, longevity does not necessarily equate to better quality of life (Statistics Canada, 2016b).

The risk of becoming frail rises with increasing age (Puts et al., 2017). Upwards of 1 million Canadians are considered frail (Hoover, Rotermann, Sanmartin, & Bernier, 2013); this value will continue to climb as almost twice that number already experience pre-frailty characteristics (Lee, Heckman, & Molnar, 2015). Canada spends \$220 billion annually on healthcare costs of which 45% are associated with those aged 65 years and above, and 20% of lifetime health care expenses accumulate during the last year of life when older adults are most likely to be frail and vulnerable (Muscedere, 2016). Exactly how many of these individuals exhibit frailty characteristics is unclear but frail older adults are believed to be the highest consumers of health care resources (Buckinx et al., 2015).

1.2. Frailty

The earliest use of the term “*frail elderly*” was published in 1953 (Drey, Pfeifer, Sieber, & Bauer, 2010) by Twefik, stating “*she needed supervision to dress and toilet and was incontinent day and night; physically she was frail*”. Almost 40 years later, Buchner and Wagner (1992) proposed a more formal definition of frailty as “*a state of reduced physiologic reserve associated with increased susceptibility to disability.*” However, the definition of frailty remains controversial as there is still a lack of consensus on what exactly comprises this geriatric syndrome (Lang, Michel, & Zekry, 2009; Mitnitski et al., 2005; Puts et al., 2017; Walston et al., 2006). This lack of consensus is due to the various physiological, psychological, social and environmental factors that influence this syndrome (Theou et al., 2011); although clinicians report that they know frailty when they see it (Roland, Theou, Jakobi, Swan, & Jones, 2013). Lack of clarity around a definition of frailty has not slowed growth in this emerging research field. Frailty publications have increased steadily from 1990-2017 (Drey et al., 2010). Frailty research now has a dedicated scientific journal, and there are a growing number of international conferences and networks of excellence aimed at addressing this geriatric syndrome.

Frailty is distinct from disability and comorbidity, as the syndrome alone is predictive of mortality, hospitalization, institutionalization, falls, and worsening health status (de Labra, Guimaraes-Pinheiro, Maseda, Lorenzo, & Millán-Calenti, 2015). Frailty is recognized as a billable health condition with its own medical diagnostic code (2017 ICD-10-CM Diagnosis Code R54). However, physicians often use this code as a last resort, when they cannot identify another diagnosis; or whom may have misdiagnosed frailty as some other health condition as they are

unable to make a definitive diagnosis without consensus support for a single diagnostic tool (McMillan & Hubbard, 2012).

Currently, there is broad support for frailty as a state of vulnerability ranging from mild to severe, caused by a reduction across various physiological systems which places the individual at increased risk for disease and disability (Borges & Menezes, 2011; Liu & Fielding, 2011; Theou et al., 2011; Xue, 2011). In the absence of a gold-standard definition, frailty is generally determined using one of two established frailty identification tools (Sternberg, Schwartz, Karunanathan, Bergman, & Clarfield, 2011); 1) the Cardiovascular Health Study-Frailty Phenotype (FP) (Fried et al., 2001a); and 2) the Clinical Frailty Scale (CFS) (Rockwood et al., 2005). Gait speed (GS) is also considered an independent criterion for frailty (Bergman et al., 2007; Buchman, Wilson, Boyle, Bienias, & Bennett, 2007; Castell et al., 2013; Van Kan et al., 2008a, 2008b, 2009).

1.3. Assessment of Frailty

The FP was developed by Fried and colleagues (2001a); it focuses on observable, physical characteristics of frailty that interact within the individual and their environment. The FP uses five indicators to describe individuals who have rapidly declining health and increased frailty. These indicators include; unexplained weight loss, self-reported exhaustion, inactivity, weak grip strength and reduced gait speed. Individuals are classified as having one of three frailty phenotypes based upon their number of indicators; non-frail (0), pre-frail (1-2) and frail (≥ 3). Pre-frail individuals have a health status that is transitioning towards frailty, while non-frail individuals are considered robust and remain functionally independent.

The CFS (Rockwood et al., 2005) was developed from an earlier Frailty Index tool (Mitnitski, Mogilner, & Rockwood, 2001). The CFS is easy to use with good construct validity for the measurement of frailty. The CFS classifies older adults across a spectrum, starting with “*very fit*” at level one and regressing toward “*terminally ill*” at level nine. Individuals are matched with the level that best describes their current health status, to reflect their level of frailty (Theou, Brothers, Mitnitski, & Rockwood, 2013). Each level has text and pictures to aid clinicians in their decision.

Self-selected gait speed is also reflective of frailty severity (Lee et al., 2017). Normal gait speed is the velocity considered the lower limit for using a crosswalk within a safe amount of time. In the United States, gait speed required to cross the street safely is 1.22 meters per second (m/sec) while only 1.07 m/sec is required in the United Kingdom (Moseley et al., 2004; Rantanen et al., 1998). Jones, Neubauer, & Jakobi (2016) proposed gait speed values of < 1.0 m/sec indicating frail, ≥ 1.0 to < 1.5 m/sec pre-frail, and ≥ 1.5 m/sec non-frail. Previous research has also identified that the FP and CFS produce inconsistent results and that a variety of tools provides a more accurate measure of frailty status (Jones et al., 2016).

1.4. Interventions to Reverse Frailty

It is apparent that there is a paucity amongst researchers when defining and identifying frailty but there is agreement that frailty is a dynamic process where individuals transition between states (i.e. non-frail, pre-frail and frail) (Roland et al., 2013). This transition is not unidirectional but rather bidirectional (Gill, Gahbauer, Allore, & Han, 2006) therefore, evidence suggests that frailty may be reversed with the right therapeutic intervention (Xue, 2011).

The design of interventions to prevent and/or delay frailty is considered a public health priority (Gine-Garriga, Roque-Figuls, Coll-Planas, Sitja-Rabert, & Salva, 2014) because they will reduce healthcare costs (Robinson, Wu, Stiegmann, & Moss, 2011) and improve quality of life for the older adult (Brown & Zenilman, 2010; Vermeulen, Neyens, van Rossum, Spreeuwenberg, & de Witte, 2011).

Research suggests exercise as an effective therapy to reverse or slow the progression of frailty (Bray, Smart, Jakobi, & Jones, 2016; Gill et al., 2006; Landi et al., 2010; Pollock et al., 1998). This is supported by a 2011 review that suggested exercise was the only intervention to consistently improve components of frailty, such as physical function and sarcopenia (Theou et al., 2011). Sarcopenia is the age-related loss of lean body mass (Evans, 1995; Rosenberg, 1989, 1997) and is closely associated with frailty. Sarcopenia may contribute to dynapenia, the age-related loss of strength, but the latter is affected by other factors, including alterations in contractile properties (Clark & Manini, 2008) and motor unit loss (McKinnon, Montero-Odasso, & Doherty, 2015). Ultimately, sarcopenia and dynapenia are believed to have a major role in the process of frailty. Suggesting that the role of exercise in combating frailty is to preserve muscle mass and strength.

Systematic reviews on exercise and frailty suggest that it is difficult to determine which characteristics of an exercise program are most effective for combating frailty (de Labra et al., 2015; Gine-Garriga et al., 2014). Variability between studies makes it challenging to determine exercise efficacy (Serra-Prat et al., 2017). Exercise intervention efficacy also includes the delivery mode (i.e. home versus clinic), types of exercises performed (Gine-Garriga et al., 2014), progression of the exercises (Sweet, Foster, McGuigan, & Brice, 2004), and the inclusion of

individuals of varying degrees of frailty (de Labra et al., 2015). Variability in frailty status among participants may make it most challenging to determine exercise recommendations. A possible solution to the inclusion of frail and pre-frail individuals into the same exercise program could be the use of frailty identification tools, both as an inclusion criteria and as an outcome measure (Theou et al., 2011). Puts et al. (2017) recognized that frailty identification tools should be used as both an inclusion and outcome criteria for intervention studies. Doing so would allow for appropriate classification of participants at enrollment and meaningful post-intervention assessment.

Good nutrition may also help to reverse frailty syndrome as research has suggested that malnutrition and frailty overlap (Laur, McNicholl, Valaitis, & Keller, 2017). This is supported by earlier research that demonstrated an increase in protein supplementation improved physical performance in frail older adults (Tieland et al., 2012). Additionally, a high quality diet, defined as consuming an adequate amount of grains, fruits, vegetables, meats, and dairy products, with modest intake of total fat, saturated fat, cholesterol, and sodium, is associated with a lower risk of frailty (Bollwein et al., 2013; Shikany et al., 2014).

1.5. Frailty in Females

Frailty is more common in females (Collard, Boter, Schoevers, & Oude Voshaar, 2012; Fried et al., 2001b; Roland, Jakobi, Powell, & Jones, 2012). A recent study compared sexes across seven different frailty scales and demonstrated that females had higher frailty scores across all age-groups (Theou, Brothers, Peña, Mitnitski, & Rockwood, 2014). Despite frailty, females live longer and this increased longevity is often the result of their ability to adapt to their physical deconditioning or lack thereof (Statistics Canada, 2016a). This phenomenon has been coined the

male-female health-survival paradox (Hubbard & Rockwood, 2011); it highlights how females are more likely to become frail sooner than males but live longer, despite poor health and physical disability. This paradox has led some researchers to classify females as both “*more frail*” (because they have poorer health status) and “*less frail*” (because they have lower risk of mortality) than males (Gordon et al., 2016).

The commonality of frailty in the female sex is believed to be attributed to the fact that females have less initial muscle mass and strength than their age-matched male counterparts (Fried et al., 2001b). The increased incidence of frailty is believed to be a result of females dropping below functional thresholds earlier than males, thus they become frail or almost frail (pre-frail) at a much earlier age (Fried et al., 2001b). Pre-frail females represent the largest demographic of older adults living with characteristics associated with frailty (Lee et al., 2015; Statistics Canada, 2016a). Interventions that focus on pre-frail females will likely have the greatest impact on reducing the number of females who become frail.

Chapter 2: Reversing Frailty

2.1 Background

According to a recent systematic review (Puts et al., 2017), there have only been 14 frailty exercise intervention studies conducted that used a frailty identification tool as both an inclusion criteria and an outcome measure. However, only four studies (Chan et al., 2012; Kwon et al., 2015; Li et al., 2010; Ng et al., 2015) included a clearly defined pre-frail population, and only one study focused exclusively on pre-frail females (Kwon et al., 2015). A recent study, not included in this systematic review, also evaluated an exercise intervention on pre-frail older adults, but not specifically females (Serra-Prat et al., 2017). These five studies report mixed results with exercise interventions to reverse frailty.

Chan and colleagues (2012) randomized 117 participants (59% female) to one of two group interventions: 1) Exercise plus nutrition; or 2) Non-exercise and nutrition. The exercise plus nutrition group exercised for one hour, three times per week for 12-weeks. The program incorporated multi-component training (MCT), inclusive of aerobic, balance, flexibility and resistance exercises. Resistance exercises comprised the majority of training time, utilizing rubber bands and water-filled bottles (0.6-1 liters). The resistance exercises targeted all major muscle groups of the upper and lower body. Participants performed 10-15 repetitions for each exercise. The nutrition component involved regular inquiry by staff about participant's dietary compliance and responding to dietary questions during the exercise program. The FP identification tool was used to classify participants; however, investigators modified the weight loss and physical activity indicators. At baseline, 102 participants were classified as pre-frail and 15 as frail. After adjusting for cognitive training within each group, the 3-month assessment showed that 45% of the exercise

plus nutrition intervention group reversed their frailty status, either becoming non-frail or pre-frail, compared to only 27% in the non-exercise and nutrition group; representing a significant between-group improvement.

Ng and colleagues (2015) performed a randomized, controlled trial with five parallel groups: 1) Physical exercise intervention; 2) Nutrition intervention; 3) Cognitive training intervention; 4) Combination intervention, which combined interventions from groups 1, 2 and 3; and a 5) Control group. The physical exercise and combination intervention groups completed 12-weeks of twice weekly, 90 minute (min), exercise classes that included resistance exercises integrated with functional tasks and balance training involving functional strength activities. Participants then completed a 12-week home-based exercise program. Resistance exercises consisted of one set of 8-15 repetitions, for 8-10 major muscle groups. The authors suggested that individual physical abilities were considered when prescribing the exercises; however, they did not describe how the program was progressed across the 12-weeks. Two-hundred and forty-six participants were classified as either frail (28%) or pre-frail (72%) using a modified version of FP tool. Modifications included having a body mass index (BMI) < 18.5 (kilograms per meter squared; kg/m²) and muscle weakness, determined using isometric knee extension strength of scores falling within the lowest quartile, based upon the individual's sex and BMI. One hundred and fifty-one participants were female (61%) but frailty classification was not split based upon sex. During the three and six-month assessment, the physical exercise and combination groups were the only two interventions to show a significant improvement in frailty status. Over 12-months, 35.6-47.8% of intervention group participants reversed (less frail) frailty status, versus only 15% of control group participants; representing a significant between-group improvement. Participants reversed their frailty score

(less frail) if they transitioned to a lower frailty category i.e. pre-frail to non-frail or frail to pre/non-frail.

Li and colleagues (2010) performed a randomized, controlled study with two groups, either a: 1) Comprehensive geriatric assessment (CGA) intervention; or a 2) Control group. The CGA intervention included a combination of medication adjustment, exercise instruction, nutrition support, physical rehabilitation, social worker consultation, and specialist referrals. The details of the exercise instruction were unclear, although the authors suggested that participants received lower extremity muscular training exercise and/or individual exercise prescriptions. Participants were classified as frail or pre-frail according to the FP. One hundred and fifty-two of the 310 total participants were randomized to the intervention group, of which 26 were determined to be frail. One hundred and forty-eight of the total participants were female although FP was not used to evaluate each sex separately. Post-trial assessments (6-months) revealed that 7.8% of intervention group participants reversed (less frail), versus 6.4% of the control group, resulting in no significant difference between groups.

Kwon and colleagues (2015) randomized 89 pre-frail females to either a: 1) Combined exercise/nutrition training group; 2) Exercise-only training group; or a 3) Control group. Exercise was one hour in length, once a week for 12-weeks. The nutrition component was a cooking class offered for one hour, once a week for 12-weeks. Participants were encouraged to perform their exercises at home in addition to the class-based program. The exercises used for resistance training were poorly described. However, the authors suggested that participants started by using their body weight as resistance and then progressed to rubber bands and dumbbells. Exercises started with one set of five repetitions and progressed to one set of ten repetitions. Pre-frail female participants

were selected using a modified version of the FP. Eighty-nine participants were assigned to one of the three groups. Only the exercise-training group showed a significant increase in grip strength and indicators of health-related quality of life, versus the control group after the 12-week intervention; however, it was unclear from the results if frailty status changed.

Serra-Prat and colleagues (2017) performed a randomized, controlled trial with two parallel arms; a 1) Nutrition and physical activity intervention group; and a 2) Control group. The physical activity component included aerobic, resistance and balance exercises. Aerobic exercise consisted of walking outdoors for 30–45 min/day at least 4 days/week. Resistance and balance exercises incorporated a set of 15 different exercises; three for strengthening the arms, seven for strengthening the legs, and five that would challenge balance and coordination. Resistance and balance exercises were completed at home for 20-25 min/day at least 4 days/week. Each exercise was performed for ten repetitions, taking approximately one min to complete. These exercises were progressed to 15 repetitions per min over a 2-3-month period, with 30 seconds (sec) rest between each exercise. Pre-frail participants were selected using the FP. One hundred and seventy-two participants were recruited and 80 were randomly assigned to the intervention group. Ninety-seven of the total participants were female with 41 in the intervention group. The follow-up assessment (12-months) revealed 21.3% of intervention group participants reversed to a non-frail phenotype, versus 15.3% of the control group; resulting in a non-significant group difference. Improvements in frailty status were not stratified by sex.

The appropriate exercise to reverse frailty status involves MCT. This type of training is suggested to be superior to other programs that focus on one type of exercise (i.e. balance) (Cadore, Rodríguez-Mañas, Sinclair, & Izquierdo, 2013; Seco et al., 2013). Pre-frail individuals are at a

critical point, where the training goal is to reverse frailty status. If they do not take preventative measures, they may regress further and become frail. Therefore, exercise recommendations suggest that MCT, with a focus on resistance and balance training, is the most effective exercise intervention for pre-frail older adults because they still possess the capacity to perform successfully (Bray et al., 2016).

Conversely, frail individuals are recommended to perform MCT but with an emphasis on aerobic training. Frail individuals have diminished aerobic capacity; therefore, the training goal is to alleviate perceptions of exhaustion associated with poor aerobic conditioning. This could potentially return these individuals to a pre-frail status and thus, permit a shift in training to focus upon resistance and balance modalities (Bray et al., 2016).

In summary, results from these exercise intervention studies are inconsistent. The only interventions found to have a significant effect on the reversal of frailty characteristics are Chan et al. (2012) and Ng et al. (2015). However, these studies used a modified FP tool so the results should be interpreted with caution (Dent, Kowal, Hoogendijk, 2016). These mixed results might also be the consequence of not separating the frailty groups by sex; females experience frailty differently than males (Fried et al., 2001b). Furthermore, exercise recommendations should differ based upon the individual's level of frailty (Bray et al., 2016). Finally, more exercise interventions need to use validated frailty tools to appropriately evaluate frailty at the onset and conclusion of an intervention (Theou et al., 2011).

2.1.1. Purpose and Hypothesis

The primary purpose of this study was to determine whether a specialized exercise program would reverse frailty in older females who are pre-frail. Secondary purposes include; determining if a specialized exercise program would improve functional task performance and muscle strength in the target population. It was hypothesized that the exercise (EX) group would have more participants reverse frailty (less frail) and fewer participants become more frail versus the control (CON) group. In addition, changes in frailty status would be related to positive changes in functional task performance and measures of knee extension (KE) and elbow flexion (EF) isometric and isotonic strength.

2.2 Methods

Participants

Participants were recruited via; advertisement brochures placed at high traffic areas where seniors congregate, letters of information about the study were sent to senior's community-groups, and presentations at local health fairs and to senior's organizations. All participants were required to read the letter of information and provide written consent prior to participating in the study. Research ethical approval was granted by the University of British Columbia Clinical Research Ethics Board (H16-00712) (Appendix A), and registered with ClinicalTrials.gov (NCT02952443) (Appendix B).

Prior to the baseline assessment, all participants were instructed to; avoid strenuous exercise for 24-hours, and asked to refrain from caffeine, smoking or alcohol consumption for two hours.

2.2.1 Assessment

Pre-Screening

Participants completed the Montreal Cognitive Assessment (MoCA; Version 7.1). The MoCA is a validated screening tool used to identify the onset of mild cognitive impairment (MCI) and the early stages of Alzheimer's-like dementia. The MoCA requires participants to answer questions that test visuospatial, naming, memory, attention, language, abstract thought, delayed verbal recall and special orientation skills. Individuals that receive a score less than 26, out of a possible 30 points may have a cognitive impairment. However, recent research suggested that the original scoring system was too stringent based upon normative data stratified by age and education (Malek-Ahmadi et al., 2015). The MoCA identifies individuals who might have difficulty learning and remembering the exercises prescribed in the intervention. The MoCA can be used in a variety of settings including primary and acute care, with culturally diverse populations, and across a variety of age groups and differing educational levels (Nasreddine et al., 2005).

Physical Activity Readiness – Questionnaire Plus (PAR-Q⁺) is a two-part questionnaire that asks individuals about their health history to determine potential risk of exercise participation. If an individual answers “yes” to any of the questions in part one then they must complete part two for further qualification of the indicated health condition. A “yes” answer to any of the nine follow-up questions in part two suggests that further medical clearance is required from either a certified exercise physiologist or physician before participation in exercise (Warburton, Bredin, Jamnik, & Gledhill, 2011).

The short-form version of the Edinburgh Handedness Inventory (EHI) (Veale, 2014) was used to determine hand dominance, while six questions (Appendix C) were used to determine leg dominance; dominance meaning the side that an individual would prefer to use for most, if not all activities. Leg dominance is commonly determined by asking which leg an individual would prefer to kick a ball (Hoffman & Payne, 1995).

Participant characteristics included; age, height in centimeters (cm), bodyweight in kilograms (kg), BMI and number of comorbidities identified via responses to the PAR-Q⁺. Height and body weight were recorded without shoes and with participants wearing light clothing. A wall-mounted stadiometer (SECA Version 206; Hamburg, Germany) assessed standing height. Participants were instructed to stand vertical, with their buttocks and upper back against the wall and look straight ahead; the measurement was taken on the exhale of their breath. Body weight was determined using a professional weigh scale (Health-o-meter 599KL; McCook, Illinois). Body mass index was determined from body weight (kg) divided by height (meters; m) squared (kg/m²).

Exclusion criteria for this study included; being male, under 65 and over 99 years of age, a MoCA score less than the normative values, stratified by age and education, proposed by Malek-Ahmadi and colleagues (2015), any major injuries or surgeries to the dominant arm or leg in the last six months and being unable to read, write and/or speak English.

Frailty

Participants were classified as pre-frail if they scored 1-2 on the FP tool or 4-6 on the CFS or recorded a GS ≥ 1.0 to < 1.5 m/sec. The FP uses five indicators to assess frailty. A score of ≥ 3 suggests that a participant is frail; a score of 1-2 identifies the pre-frailty phenotype; and a score

of zero indicates that an individual is non-frail (Fried et al., 2001a). The components of the FP assessment and respective cut-off values include:

1) Unexplained weight loss (i.e. not due to dieting and/or exercise) of more than ten pounds (lbs) or 4.5 kg in the last year receives a score of one;

2) Self-reported fatigue as determined by two questions; i) *“How often in the last week did you feel that everything you did was an effort?”* and ii) *“How often in the last week did you feel that you could not get going?”* A “yes” response to either question receives a score of one;

3) Physical activity energy expenditure less than 270 kcal per day, as determined by the Minnesota Leisure Time Physical Activity Questionnaire (MLTPAQ) receives a score of one;

4) Grip strength below specific cut-points relative to individual BMI (kg/m^2) receives a score of one; BMI ≤ 23 and grip $\leq 17\text{kg}$, BMI 23.1-26 and grip $\leq 17.3\text{kg}$, BMI 26.1-29 and grip $\leq 18\text{kg}$, or a BMI > 29 and grip $\leq 21\text{kg}$;

5) Gait speed as time to walk a 15-foot (4.6 m) straight course relative to stature receives a score of one; height ≤ 159 cm and gait speed ≥ 7 sec or height > 159 cm and gait speed ≥ 6 sec.

Frailty status was also assessed using the CFS through examination of the participant’s current health and functional status (Rockwood et al., 2005). The CFS uses both visual and text descriptions across a spectrum of nine levels of frailty:

Level 1) Very Fit – robust, active and energetic; exercises regularly; most fit for their age

Level 2) Well – without active disease but less fit than level 1; very active occasionally

Level 3) Managing Well – medical problems are well controlled; not regularly active beyond walking

Level 4) Vulnerable – not dependent on others; symptoms limit activities; common complaint is “*slowed up*” and/or being tired during the day

Level 5) Mildly Frail – more evident slowing; need help in high order instrumental activities of daily living; impairment in shopping, walking outside alone, meal preparation and housework

Level 6) Moderately Frail – need help with all outside activities, keeping house, bathing and dressing; problems with stairs

Level 7) Severely Frail – dependent for personal care from whatever cause but stable and not at risk of dying

Level 8) Very Severely Frail – completely dependent; approaching end of life; typically, will not recover from a minor illness

Level 9) Terminally Ill – life expectancy < 6 months

Previous investigations have suggested that the FP and CFS do not always provide the same results and using several frailty tools may provide a more reliable measure of frailty (Jones et al., 2016). Therefore, GS was used as a third measure to qualify frailty status. Participants were given two

trials to walk a measured 8 m straight distance on a non-carpeted floor (Figure 2.1). Participants started with the toes of both feet on the start line. On the command of “go,” the participant was instructed to walk to the finish line at a self-selected walking speed that the participant considered normal, as if they were “walking down the street to go to the store.” This definition of normal walking speed has been previously utilized in other established gait speed tests (Guralnik et al., 1994). The participant starts at point one and ambulates 2 m to accelerate GS to a normal pace. The timer (iPhone 5C, Apple, Cupertino, CA) was started when the participant crossed point two and continued walking for 4 m. The timer was stopped when the participant crossed point three; however, the participant continued walking until point four, an additional 2 m so that they could decelerate their GS to a stop. Providing participants with an appropriate acceleration and deceleration phase provides a more acute measure of “true” GS. Participants were blinded to when they were timed during the GS assessment. The GS test was completed twice to promote familiarity and improve accuracy in determining true normal GS. The fastest normal walking speed was recorded and used for data analysis. Frailty status was determined using GS cut-offs proposed by Jones and colleagues (2016); frail < 1.0 m/sec; pre-frail ≥ 1.0 to < 1.5 m/sec; non-frail ≥ 1.5 m/sec. GS results were also used as measure of functional task performance.

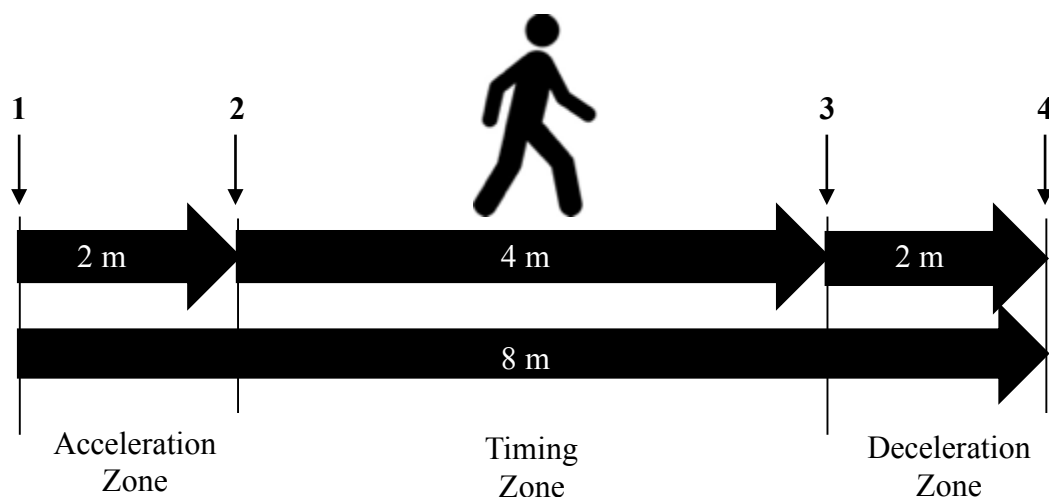


Figure 2.1 Evaluation of gait speed. Point one indicates where participant started walking; point two indicates where the timer started; point three indicates where the timer stopped; point four indicates where the participant stopped walking. m = meters.

The fifth indicator of the FP tool is also a measure gait speed. Rather than repeat a similar gait speed assessment, the results from our GS test were used to determine if a participant met the criteria for the FP gait speed frailty indicator. This was completed using the following height stratified ($>$ or \leq 159 cm) equations:

1) Length of course = 15 feet = 4.572 m

<p>Time to complete if \leq 159 cm = 7 sec</p> $\frac{4.572 \text{ m}}{7 \text{ sec}}$ <p>= 0.653 m/sec</p>	<p>Time to complete if $>$ 159 cm = 6 sec</p> $\frac{4.572 \text{ m}}{6 \text{ sec}}$ <p>= 0.762 m/sec</p>
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Equation 2.1 Calculation for converting the FP gait speed indicator to m/sec.

2) The fastest m/sec GS time for each participant was compared to the appropriate height categorical cut-off time; 3) Participants with a GS \leq the cut-off received a score of one for the FP gait speed indicator. For clarity, see the following fictitious example:

Participant A:

- Height = 160 cm
- Time to complete walking course = 7 sec
- Length of our GS course = 4 m
 - Converted to m/sec = 4 m / 7 sec = 0.571 m/sec

- FP m/sec cut-off value for participant with a height > 159 cm = 0.762 m/sec
- 0.571 m/sec is < or slower than 0.762 m/sec
- Therefore, participant receives a score of “one” according to the FP gait speed indicator

Functional Task Performance

Handgrip strength has been shown to be an accurate measure of total body strength (Wind, Takken, Helder, & Engelbert, 2010). Participants were positioned with a hand dynamometer (Baseline Smedley, Fabrication Enterprises Incorporated, White Plains, NY) at arm’s length, slightly abducted from the side of the torso. Participants were instructed to squeeze the dynamometer as hard as possible and exhale for three sec. The order of testing for the dominant and non-dominant hand was randomized and trials occurred between gait tests to minimize fatigue and a learning effect. However, participants performed two trials to promote accuracy. The highest score was recorded and used for data analysis as a measure of functional performance, and within the FP tool.

Chair sit-to-stand (STS) time is indicative of leg strength and time to complete has been correlated with frailty status (Batista et al., 2012). The chair STS task was adopted from the short physical performance battery (SPPB) protocol; the only modification being the time to complete and not the SPPB specific scoring system was used for data analysis. The SPPB protocol is a standardized performance test applied in research and geriatric settings. The SPPB can characterize older adults across a broad spectrum of lower extremity function (Guralnik et al., 1994). The chair STS task requires participants to stand from a chair of standard height (45.7 cm) with their arms folded across their chest. If the participant completes this task safely, they then perform the repeated STS

task. Participants stand and then sit-down until their buttocks touches the chair, repeating until five STSs are completed.

Isometric and Isotonic Strength

The Biodex Dynamometer System 4 Pro (Biodex Medical Systems Incorporated, Shirley, NY) was used to determine peak torque, measured in newton meters (Nm) during isometric contractions and peak velocity, measured in degrees per second (°/sec) during isotonic contractions, while performing KE and EF. KE and EF were selected because previous research in fatigability have utilized identical movements, demonstrating that they are safe for older adults (Dalton, Power, Paturel, & Rice, 2015; Dalton, Power, Vandervoort, & Rice, 2012; Yoon, Doyel, Widule, & Hunter, 2015; Yoon, Schlinder-Delap, & Hunter, 2013). Additionally, both movements have functional application; KE is performed when standing up from a toilet or picking up an object from the ground; EF is performed when drinking from a cup; EF muscles may also be recruited when carrying an object due to coactivation (Le, Best, Khan, Mendel, & Marras, 2017).

Knee Extension

Knee extension primarily requires activation of the quadriceps muscles (vastus lateralis, vastus medialis, vastus intermedius, and rectus femoris). Participants were positioned in the Biodex Dynamometer System 4 Pro chair with the lateral femoral condyle of the dominant leg aligned with the dynamometer center of rotation. The distal end of the KE limb attachment was secured to the ankle of the participant, just superior to the lateral malleolus (Perry, Carville, Smith, Rutherford, & Newham, 2007). Participants were secured to the dynamometer via restraining straps that crossed between the shoulder and opposite hip on each side. A third strap was secured

across the thigh of the tested leg (Figure 2.2). To account for the effect of gravity, the weight of the limb was calculated by the Biodex. The calculation was performed with the knee extended to 160 degrees ($^{\circ}$); 180 $^{\circ}$ represented terminal KE. One hundred and sixty degrees was used for limb weight because it was the maximum degree of KE that the participant performed as part of the protocol and thus, represented when gravitational pull was greatest; this was confirmed during pilot testing. Ninety degrees, the point at which the lower leg is perpendicular to the floor, represented the point of reference for the determination of 160 $^{\circ}$. Ninety degrees was measured with a goniometer, with the axis of rotation being the lateral femoral condyle and the midline of the femur and lower leg serving as the points of reference for the goniometers arms.



Figure 2.2. Knee extension set-up.

The participant was positioned with their hips flexed between 95 and 105° (Dalton et al., 2012), as determined by goniometer measurement, with the greater trochanter as the axis of rotation and the midline of the trunk and femur serving as the points of reference for the goniometer arms. Participants crossed their arms over their chest while performing contractions. All variables, such as chair and dynamometer height, were recorded and replicated during intra and follow-up assessments. A full-list of controlled variables is provided in Appendix D.

Elbow Flexion

The muscles primarily involved in EF are the brachioradialis, biceps brachii, and brachialis. Participants rested their feet on a pedal at a height that placed their hip flexion between 95 and 105° (Figure 2.3). The trochlea and capitulum of the elbow was aligned with the dynamometer center of rotation. An elbow attachment secured the participants arm, provided support throughout the entire EF movement and kept the shoulder height level with the unsupported arm. The elbow support attachment moved to support different arm lengths.

With the elbow fully supported limb weight was not required as gravity had little effect. The participant's hand was set to a neutral position; this was the most comfortable position for participants as determined by pilot testing. Participants placed their non-dominant hand on the opposite shoulder and the upper body was secured using restraining straps, as described for the KE protocol. Elbow flexion of 90° served as the point of reference, as determined by goniometer measurement with the capitulum and trochlea as the axis of rotation and the midline of the upper and lower arm serving as the points of reference for the goniometer arms. All variables, such as chair and dynamometer height, were recorded and replicated during intra and follow-up assessment. A full-list of controlled variables is provided in Appendix D.



Figure 2.3 Elbow flexion set-up.

Isometric Contractions

The participant's knee and elbow angle were set to 90°. Prior to starting isometric contractions, the participant was instructed to extend their knee or flex their elbow “*as hard and as fast as possible*” for five sec. Participants completed five contractions for both KE and EF, with an inter-contraction rest time of 120 sec. All isometric values were recorded in a unique participant file using the Biodex Advantage software program. The highest output was used for data analysis.

Isometric contractions are considered a standard for measuring power output, as noted by their inclusion in a large number of protocols (Christie, Snook, & Kent-Braun, 2011). Isometric

contractions were also performed because research has demonstrated that older adults experience a slowing in their rate of isometric force production (Klass, Baudry, & Duchateau, 2008; LaRoche, Knight, Dickie, Lussier, & Roy, 2007). Additionally, older adults become less fatigued from such contractions until advanced ages (Dalton et al., 2015), leading researchers to believe that participants would still be capable of performing isotonic contractions maximally. Isometric contractions were also performed first because their outputs dictated the resistance used for isotonic contractions.

Isotonic Contractions

Participants were required to move 20% of the peak torque, obtained during isometric contractions, for isotonic contractions. The 20% of peak torque was calculated using the following formula:

$$\text{Peak Torque} \times 0.20 = \text{Isotonic resistance}$$

$$\text{Example} = 106 \times 0.20 = 21.2 \text{ Nm}$$

Equation 2.2 Calculation for isotonic resistance.

In all cases, resistance was rounded down to the nearest available setting to ensure that participants were contracting no more than 20%. Additionally, during all follow-up assessments, isotonic resistance was set at the 20% obtained during the initial visit, allowing for direct comparisons between isotonic contractions over time.

Isotonic contractions were performed through 70° range of motion (ROM); starting position of the knee and elbow angle were 90 and 160°, respectively. Participants were instructed to contract “*as hard and as fast as possible.*” Participants completed five contractions for both KE and EF, with

an inter-contraction rest time of 120 sec. All isotonic values were recorded in a unique participant file using the Biodex Advantage software program. The highest output was used for data analysis.

Isotonic contractions were selected in favor of isokinetic because they relate to normal functional movements; work against fixed resistances with varying velocities. Additionally, research suggests that older adults may experience limitations with higher isokinetic velocities (Lanza, Towse, Caldwell, Wigmore, & Kent-Braun, 2003).

Timeline

All assessment measures were completed at week 0 (baseline) and at week 13 (follow-up) for both the EX and CON group. Intra-experimental tests were also repeated at weeks five and nine for only the EX group. These extra assessments helped to determine the ideal time required for functional task performance and muscle strength changes to occur in this population.

2.2.2 Experimental Set-up and Procedure

Participants who were pre-frail were assigned to either the EX or CON group. Random assignment was not possible as all potential participants conveyed that they wanted to have the choice for the arm of the study they would follow (EX or CON). Many participants did not want to join the EX group because of the time commitment. The EX group completed a 12-week exercise program which followed established guidelines (Figure 2.4) for exercise frequency (3-days/week), duration (45-60 min/session), intensity (80% of estimated one-repetition maximum or 3-4 rating of perceived exertion; RPE) and type (primarily resistance and balance exercises). The EX group was divided into two separate exercise groups; 1) morning (10-11 am) and 2) afternoon (1-2 pm) based-

upon room size and participant availability. The CON group was asked to maintain their normal routine for the duration of the intervention (12-weeks).

The exercise program was divided into three phases (Figure 2.5): Phase one was aerobic warm-up; Phase two was resistance and balance exercises; and Phase three was flexibility cool-down. Each phase of the exercise program was designed to address the unique needs associated with the pre-frail phenotype.

Phase one was ten min in length. Participants were given a choice between using an elliptical, treadmill, stationary bike, or marching in place. A complete list of equipment used in the exercise program is provided in Appendix E. Participants reported their level of exertion, using the Rating of Perceived Exertion CR-10 scale (Borg 1982), five and ten min into the aerobic warm-up; this ensured they reached the desired intensity (RPE 3-4 or moderate-vigorous).

Phase two was 45 min in length. Resistance training was divided into three blocks of four weeks (Figure 2.6). Participants started training with 2-3 sets and 8-12 repetitions during weeks 1-4 (block one). Participants progressed to three sets during the second or third week depending on individual ability. Participants started with two sets as there was a risk that three sets might have increased the risk of post-exercise muscle soreness. This may have become a barrier to further participation early in the intervention. In block two, the repetition range decreased to 6-10, and later reduced to 4-8 during block three (weeks 9-12).

Repetition range was altered to adhere to the training principle of progression and because lower repetitions with greater intensity (i.e. heavier weight) will lead to a greater increase in strength than higher repetitions with less intensity (i.e. lighter weight) (Campos et al., 2002; Schoenfeld et.

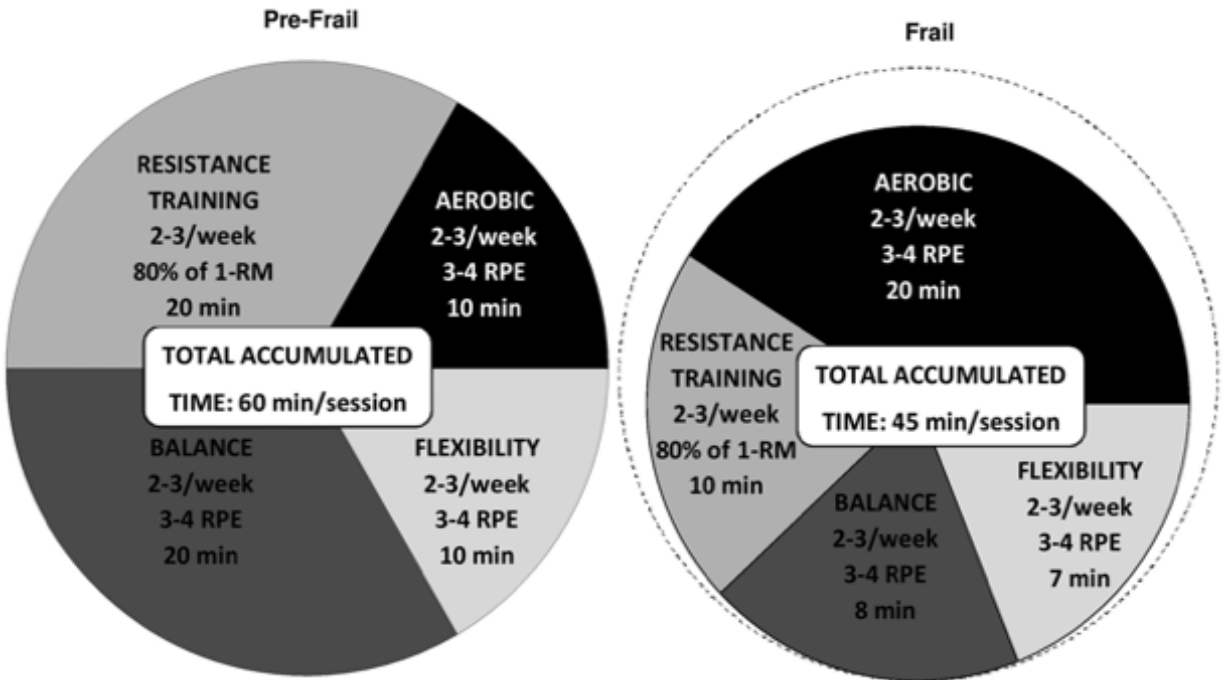


Figure 2.4 Exercise prescription for pre-frail and frail older adults (adapted from Bray et al., 2016).

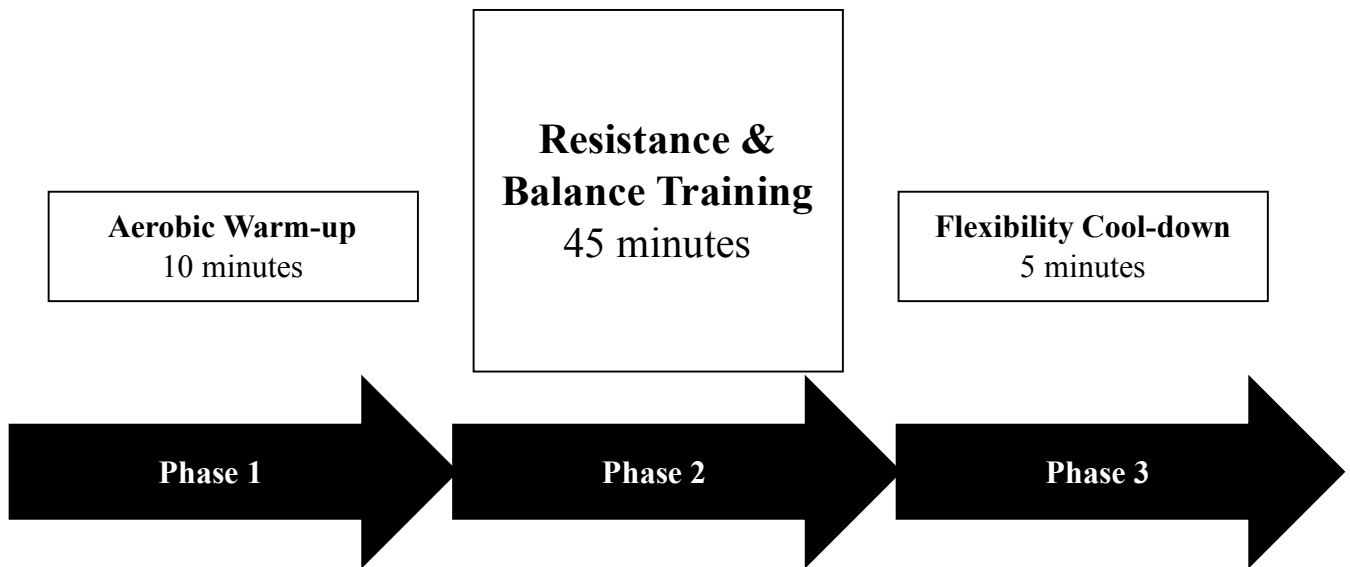


Figure 2.5 Overview of an exercise session.

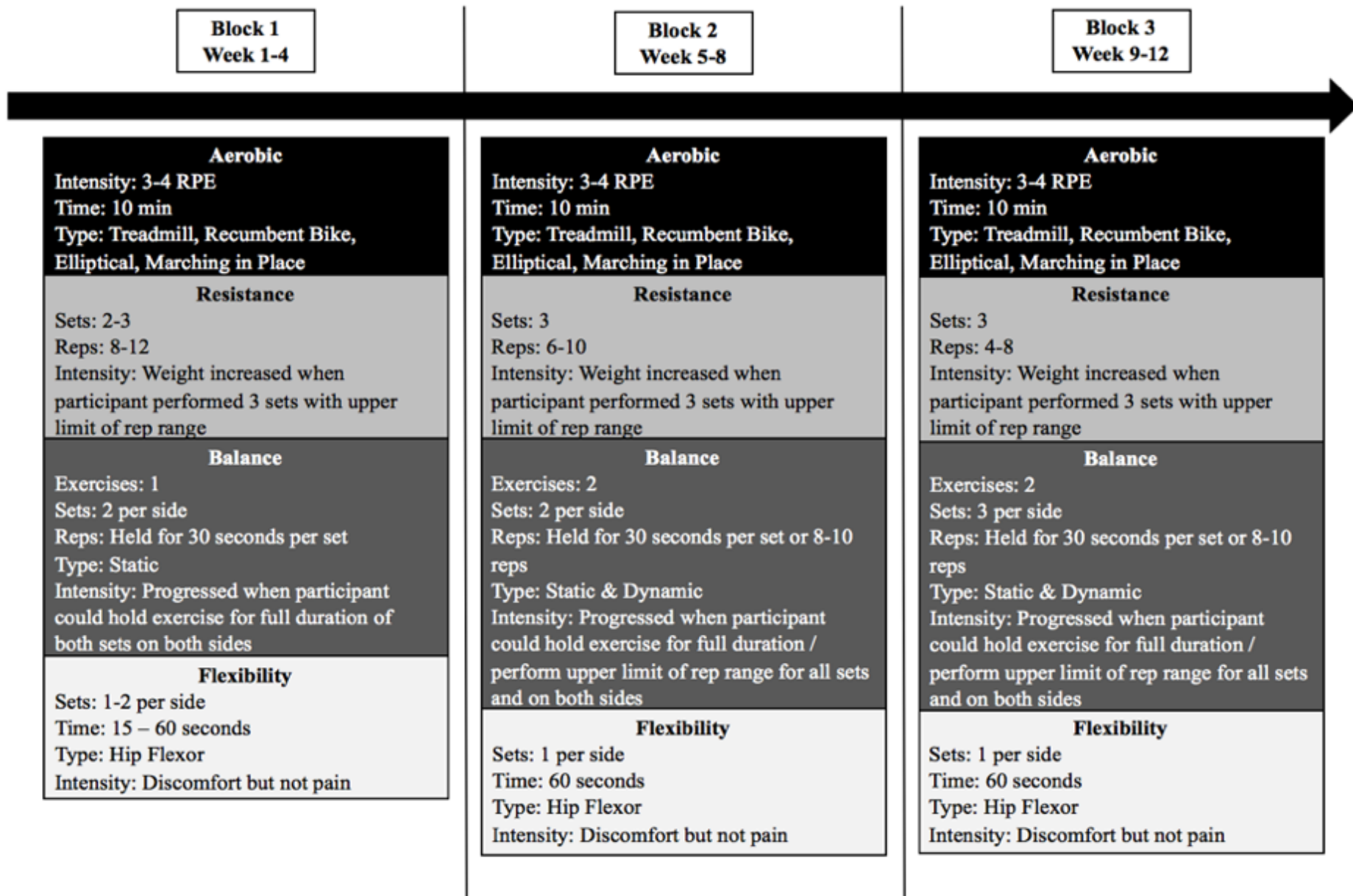


Figure 2.6 Overview of the exercise program and progression of exercises.

al., 2014). The training principle of progression states that if an individual is to continue producing higher levels of performance, the intensity of the training program must become greater to cause a positive training adaptation.

Each training block built upon the previous block and had the following goals: 1) Build technical movement confidence using lighter weights in block one; 2) Transitioning to heavier weights and fewer repetitions in block two; and 3) Focus on building strength in block three.

Four resistance exercises were selected: 1) Squat; 2) Bench press; 3) Deadlift; and 4) Inclined leg press (Fig 2.7-2.10). These exercises were preferred because of their functional application. The squat replicates standing-up from a squatting position (i.e. a toilet) and builds lower body strength by targeting the quadriceps, gluteus maximus, hamstrings, adductor magnus, gastrocnemius and soleus muscles. The deadlift imitates picking-up a weighted object from the ground (i.e. shopping bag) and builds overall body strength by targeting several muscles including; the erector spinae, gluteus maximus, hamstrings, quadriceps, portions of the trapezius and rectus abdominis muscles. The bench press replicates carrying or pushing an object (i.e. pushing open a door) and builds upper body strength by targeting the pectoralis muscle group, parts of the deltoids, and triceps muscles. These open-chain exercises were performed using free weights such as dumbbells, barbells and weighted plates. The inclined leg press was used as a supplement exercise to the squat as it mimics the movement pattern and targets the same muscles but is considered a closed-chain movement. Closed-chain exercises require individuals to move through a set ROM or fixed space, as opposed to an open-chain exercise where the arm or leg is free to move. Having a fixed ROM for the inclined leg press allowed participants to lift more weight, safely, than when performing

the open-chain squat movement. This may have allowed participants to achieve greater gains in leg strength compared to using only the squat exercise.

Participants used the OMNI – Resistance Exercise Scale (OMNI-RES) to evaluate work intensity of the last set, for every resistance exercise, during each session. The OMNI-RES provides a reliable measure of work intensity in older adults performing resistance training exercises (Gearheart et al., 2009).



Figure 2.7 Goblet squat variation.



Figure 2.8 Bench press.



Figure 2.9 Deadlift.



Figure 2.10 Inclined leg press.

During each bout of resistance training participants were separated into two groups of 2-3 individuals. Each group started with the squat or bench press and finished with the deadlift or inclined leg press. This ordering of exercises allowed participants to circulate efficiently between apparatuses.

Rest periods between sets ranged from 1-3 min. As one participant performed a set, the other individuals rested. When a participant completed a set, the weight was adjusted for the next participant and then they performed their set. This rotation continued until all sets were completed for an exercise. Participants would then move to the next exercise. Therefore, the time between sets was dictated by the time it took participants to complete a set and change the weight.

In accordance with the training principle of overload, weight increased when participants reached the upper limit of the repetition range for a particular training block; the principle of overload

requires assigning a workout or training regime of greater intensity than an individual is accustomed. If a participant performed three sets of 12 repetitions during block one then more weight was added to that exercise during the next session. The participant would then revert to three sets of eight repetitions and gradually build towards three sets of 12 repetitions, where they increased the weight again. The weight that would be added to an exercise, when a participant had reached the upper limit of a repetition range for all sets was intended to be 2.5lbs for bench press, and 5-10lbs for the squat, deadlift and/or inclined leg press.

Participants were also instructed to increase the number of repetitions performed for each exercise during every session. For example, if a participant performed three sets of eight repetitions during block one they were then instructed to perform three sets of nine repetitions during the next training day. The repetition progression was determined by the investigator for each individual participant. However, RPE aided researchers in determining how many repetitions to instruct participants to perform.

Not all participants were capable of starting an exercise with weight, moving through the desired ROM and/or progressing at the same pace. Each participant had unique abilities therefore, a modified version of the exercise ensured participant safety and that they remained confident in their abilities. All participants began with the easiest modification for each exercise. When the participant had demonstrated they could safely and effectively perform the modified exercise they were then progressed to a more challenging version; such modifications obey the training principle of individuality, which states that all individuals have unique abilities and needs. For example, a participant that could not squat to the lowest box (i.e. 12 inches; ") would start by squatting to a high box (i.e. 24"). Once the individual demonstrated that they possessed the strength and ability

to perform a squat to a high box, for the block specific upper limit of the repetition range for all sets, the box would be lowered (i.e. 18"). The box was incrementally lowered until the participant could squat to the lowest box, at which point weight would be added. The lowest box represented a parallel position for most participants, meaning the hip crease was in line with the knee. Custom-built boxes were used as a guide for participants when squatting, for the duration of the program; participants would squat down until their buttock touched the box and then returned to an erect position.

Resistance training was the most important training modality because of the positive impact it has upon building strength, an important exercise component for reversing pre-frailty. A list of all exercises and their modifications are included in Appendix F.

Balance training included one static exercise during block one and one static and dynamic exercise during block two and three. Depending upon individual ability, participants started with different balance exercises and progressed accordingly. For example, a participant could start with tandem stance (heel to toe) and progress to balancing on one leg once they performed the block specific upper limit of the repetition range for all sets, on both sides, without losing balance.

Dynamic balance exercises were introduced during training block two. Like the static balance exercises, dynamic balance exercises were prescribed based upon individual ability and progressed through blocks two and three accordingly. For example, a participant commenced with weight shifts and then progressed to step overs once they performed the block specific upper limit of the repetition range for all sets, without losing balance (Appendix F).

Each exercise session concluded with hip flexor flexibility training using a modified version of the protocol described by Watt and colleagues (2011). Participants that could not or did not want to perform the exercise from a kneeling position completed the standing version (Figure 2.11). Participants started the program by stretching for one 15 sec set per side, eventually progressing to 60 sec.



Figure 2.11 Kneeling and standing hip flexion stretch.

Data Analysis

Baseline characteristics were compared using an independent sample t-test.

Individual participant frailty scores were determined for each identification tool and analyzed separately. Therefore, it was possible for a participant to reverse their frailty score on one tool, yet

decline on another. For all frailty identification tools, a participant “*reversed*” their frailty status if they received a better (less frail) score at follow-up. Conversely, participants “*declined*” or remained “*unchanged*” if they received a worse (more frail) score or their values remained the same at follow-up. For each frailty identification tool, the number of participants who either reversed or declined within both the EX and CON group was determined and converted into a percentage score.

Group frailty scores, functional task performance values, KE and EF isometric and isotonic strength results were compared at baseline and follow-up for both the EX and CON groups using a two-way mixed analysis of variance (ANOVA). The primary independent variables in each model included treatment group, time, and group time interaction. Where the group time interaction was significant, tests for simple main effects were performed via a one-way ANOVA for each separate between (group) and within (time) subjects’ factors. Where the group time interaction was not significant, main effects were interpreted for the between and within-subjects’ factors.

Only the EX group was examined over time (baseline, week five, week nine, follow-up) for functional task performance, as well as KE and EF strength (isometric and isotonic) using a one-way repeated measures ANOVA. Sphericity was assessed via Mauchly’s test of sphericity; sphericity was violated if $p < 0.05$. A Greenhouse-Geisser correction was applied if sphericity was violated (Maxwell & Delaney, 2004). A Bonferroni correction was applied for confidence interval (CI) adjustments in post-hoc comparisons (Maxwell et al., 2004).

Normality was assessed via a Shapiro-Wilk’s test; it was violated if $p < 0.05$ (Thode, 2002). Homogeneity of variances was assessed using Levene’s test of equality of error variances; it was

violated if $p < 0.05$ (Levene, 1960). Homogeneity of covariance was assessed via Box's test of equality of covariance matrices; it was violated if $p < 0.001$ (Tabachnick, Fidell, & Osterlind, 2001). Data was normally distributed, and there was homogeneity of variances and covariance unless otherwise stated. Data that violated normality and homogeneity of variances was transformed using the function Log^{10} , unless otherwise stated. Statistical significance was set at $p < 0.05$. All values were reported as mean \pm standard deviation, unless otherwise stated.

Finally, a Spearman's rank-order correlation assessed the relationship relative to the difference in change between baseline to follow-up for all frailty identification tools (FP, CFS, GS), functional performance tests (grip strength and STS time), and measures of KE and EF isometric and isotonic strength. All relationships were monotonic, as assessed by visual inspection of a scatterplot, unless otherwise stated. Statistical significance was set at $p < 0.05$.

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 24 (IBM SPSS Statistics, IBM Canada Ltd. Markham, Ontario).

2.3 Results

Participants

Fifty-seven potential participants expressed interest in participating in this study, 53 met the inclusion criteria. All eligible participants were contacted but only 21 agreed to complete the baseline assessment. Lack of time to commit to the thrice-weekly exercise sessions was the primary reason to decline participation in the study ($n = 32$). One potential participant failed the pre-screen, resulting in 20 eligible participants for this study (Figure 2.12).

Three CON group participants were unable to complete the follow-up assessment at the required date because of fall-related injuries (n = 2) or illness (n = 1). One EX group participant completed < 65% of the exercise classes due to illness (seasonal flu) and therefore, was removed from the final analysis. Adherence rates for the EX group was 88.3% (89.4% am class; 86.5% pm class).

Three EX participants reported injuries prior to the intervention that required specific accommodations during the program. One participant had a previous shoulder injury that prevented them from performing the bench press exercise. One participant had abdominal surgery (> one year prior to baseline) and another had chronic lower back pain (> one year prior to baseline) that required both to have adjustments made to their squat, deadlift and inclined leg press exercises.

Participant characteristics at baseline are included in Table 2.1. There were no significant differences between groups except for STS time. Youngest and oldest age was 65 and 81 years, respectively. Smallest and largest BMI was 18.3 and 39.7 kg/m², respectively. The number of comorbidities ranged between 1-3 per participant in both the EX and CON groups and included; macular degeneration, hyperthyroidism, chronic bladder infection, diabetes, hypertension, osteoarthritis, gastroesophageal reflux disease, atrial fibrillation, stiff left ventricle, bladder weakness, arthritis, glaucoma, various chronic injuries (i.e. shoulder, back, etc.) and acid reflux.

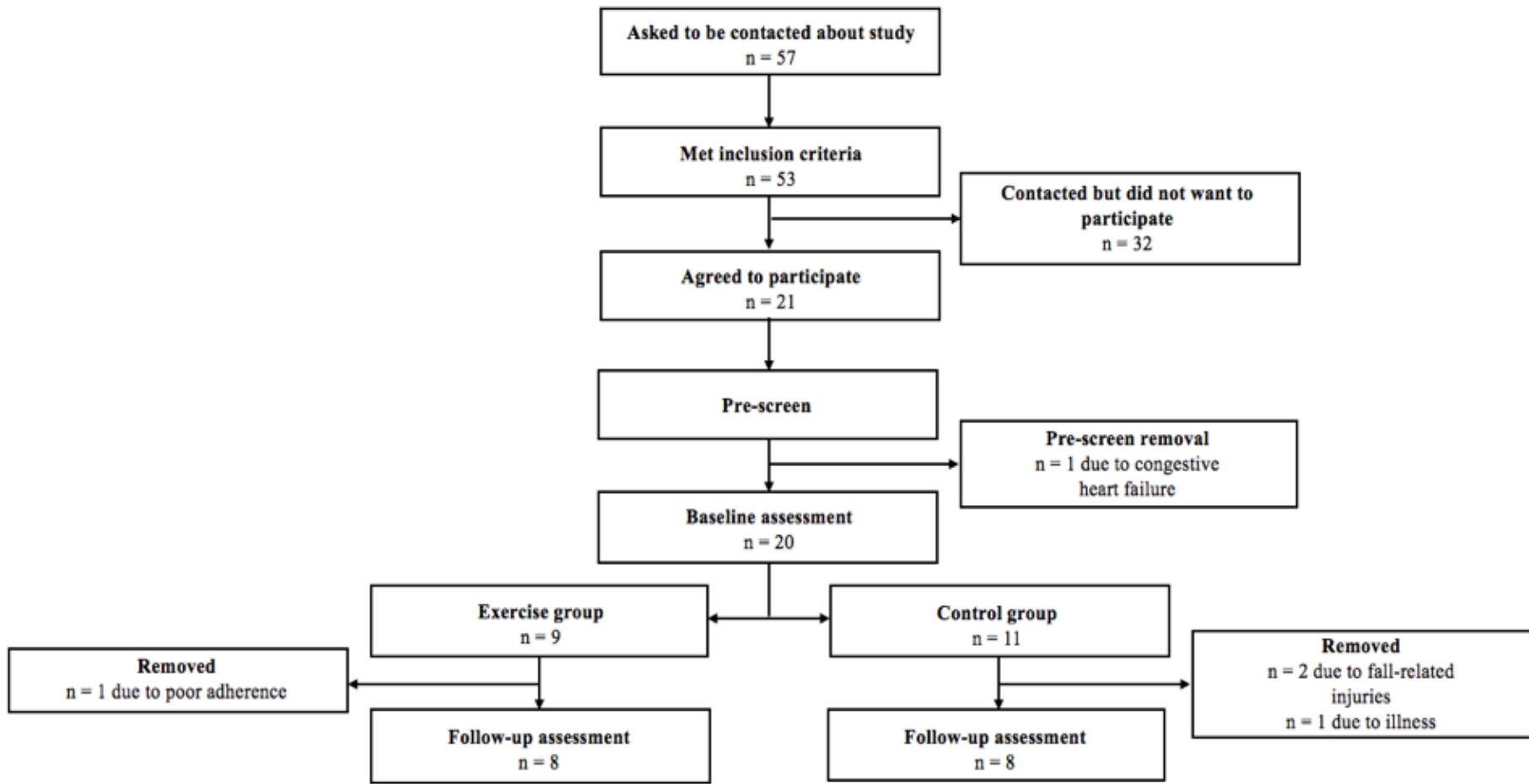


Figure 2.12 Participant enrollment and removal; as well as number of participants that completed assessments.

Table 2.1 Participants' characteristics at baseline (N = 16).

Characteristics	CON n = 8	EXP n = 8
Age (Years)	72.4 ± 5.4	72.9 ± 4.8
Height (cm)	156.4 ± 7.7	162.5 ± 4.0
Weight (kg)	67.1 ± 11.0	75.8 ± 23.3
BMI (kg/m ²)	27.4 ± 4.0	28.6 ± 8.5
MoCA	25.6 ± 2.6	25.0 ± 3.0
Comorbidities per Participant	1.9 ± 1.5	2.1 ± 1.2
<i>Frailty Status</i>		
FP	0.5 ± 0.5	1.1 ± 1.0
CFS	2.8 ± 1.0	3.4 ± 1.2
Gait Speed (m/sec)	1.2 ± 0.2	1.1 ± 0.3
<i>Functional Tasks</i>		
Grip Strength (kg)	24.2 ± 3.4	24.9 ± 4.7
STS Time (sec)	11.4 ± 2.8	15.2 ± 2.9
<i>Strength Measures</i>		
KE Isometric (Nm)	113.4 ± 17.7	100.9 ± 32.4
KE Isotonic (°/sec)	319.9 ± 42.4	302.6 ± 40.5
EF Isometric (Nm)	32.3 ± 5.2	32.3 ± 8.9
EF Isotonic (°/sec)	191.2 ± 38.2	188.2 ± 53.0

Note: Values are means ± standard deviation. CON = control; EX = exercise; BMI = body mass index; MoCA = Montreal Cognitive Assessment; FP = Frailty Phenotype; CFS = Clinical Frailty Scale; GS = gait speed; KE = knee extension; EF = elbow flexion; cm = centimeters; kg = kilograms; kg/m² = kilograms per meter squared; m/sec = meters per second; sec = seconds; Nm = newton meters; °/sec = degrees per second.

Frailty

All EX group participants showed reversal in frailty status in at least one frailty identification tool. Only two CON group participants showed no change in frailty status in at least one frailty identification tool.

The EX group FP score reversed (less frail) from 1.1 to 0.3; CFS score reversed (less frail) from 3.4 to 2.9; and GS increased (less frail) from 1.1 to 1.3 m/sec. The CON group FP score also reversed (less frail) from 0.5 to 0.3; CFS score reversed (less frail) from 2.8 to 2.7; but GS remained unchanged at 1.2 m/sec. There was a main effect for time for the FP ($F(1,14) = 8.5, p \leq 0.01$, partial $\eta^2 = 0.4$; a small to medium effect size) and CFS scores ($F(1,14) = 4.8, p \leq 0.05$, partial $\eta^2 = 0.3$; a small to medium effect size) from baseline to follow-up. However, FP violates the assumption of normality and could not be transformed using Log¹⁰.

In comparison to the CON group, the EX group had more participants reverse their frailty status for all three frailty identification tools. For the FP, 62.5% of the EX group participants reversed (less frail) their frailty status versus only 37.5% of the CON group. For the CFS, 75% of the EX group participants reversed (less frail) their frailty scores versus only 37.5% of the CON group. For GS, 100% of the EX group participants recorded a faster (less frail) GS versus only 37.5% of the CON group.

Only one participant in the EX group declined (more frail) as per their follow-up CFS score, which changed from 2.5 to 3. The CON group had 12.5 and 25% of participants decline (more frail) in their FP and CFS scores, at follow-up. In addition, 62.5% of CON participants recorded a slower GS (more frail) at follow-up. Figure 2.13 summarizes changes in frailty scores, for each frailty identification tool, for each EX and CON group participant between baseline and follow-up.

Functional Task Performance

The results of functional task performance assessments are included in Figures 2.14-2.16. A shoulder injury, unrelated to the exercise program precluded one EX group participant from

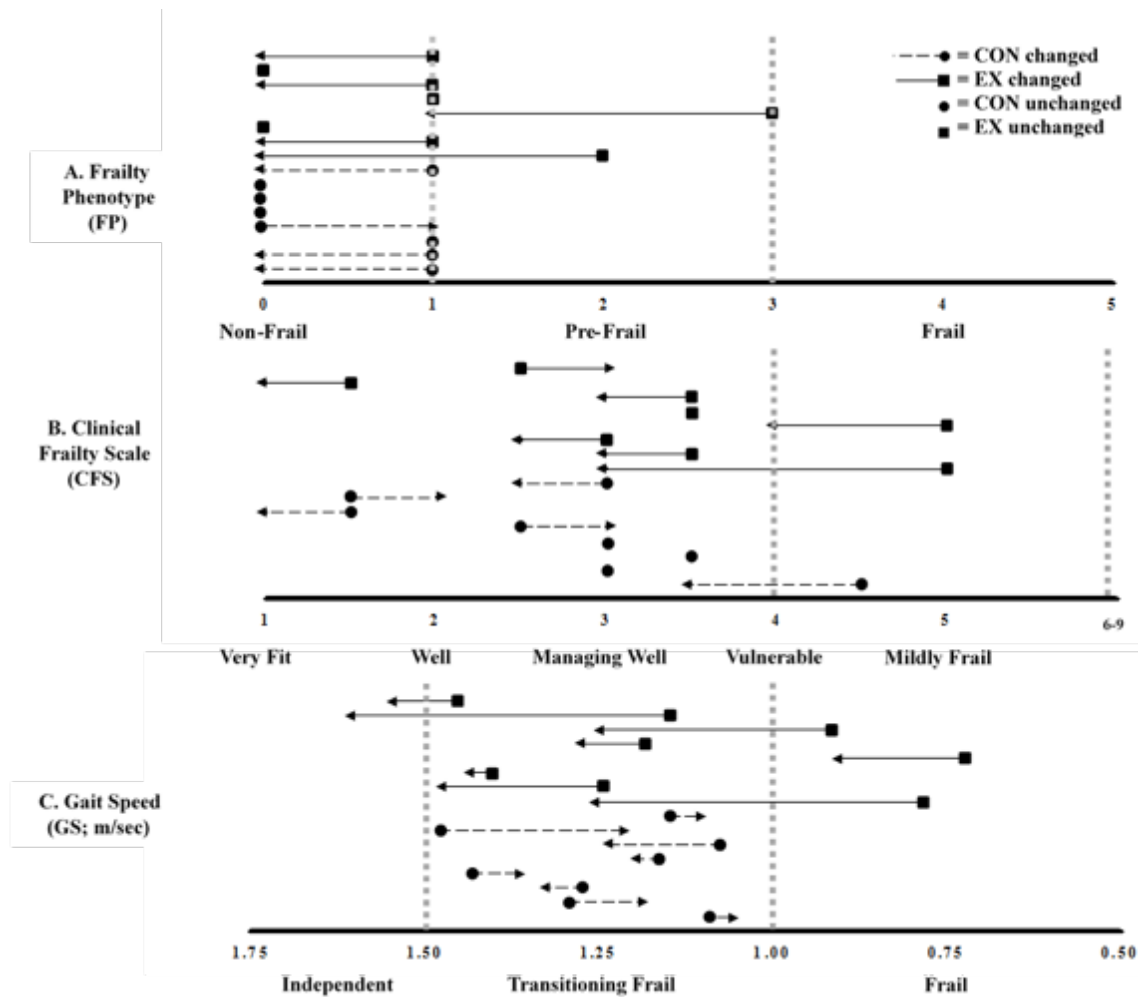


Figure 2.13 Changes in frailty status across three frailty identification tools; the Frailty Phenotype (n = 16), Clinical Frailty Scale (n = 16) and gait speed (n = 16). The presentation order of participants is consistent between each figure. Pre-frailty thresholds indicated by the vertical broken lines. The closed square with solid line = Exercise (EX) participant and direction of change; closed circle with dashed line = Control (CON) participant and direction of change; a closed square with no line = EX participant who did not change; a closed circle with no line = CON participant who did not change; m/sec = meters per second.

completing the grip strength and STS task; the participant could not place their hands across their chest without shoulder pain. There was an improvement for GS within the EX group from baseline to follow-up ($F(1, 7) = 15.2, p \leq 0.01$, partial $\eta^2 = 0.7$; a medium to large effect size). Additionally, there was an increase of 0.21 m/sec, 95% CI [0.0, 0.4], $p = 0.03$ in the EX group GS from week five (1.1 ± 0.2) to follow-up (1.3 ± 0.2). There was no statistically significant difference in the CON group's GS between baseline and follow-up.

Improvements in grip strength of 3.1 kg, 95% CI [0.2, 5.9], $p = 0.04$ were observed between baseline (24.9 ± 4.7 kg) and week nine (28.0 ± 5.9 kg). Grip strength also increased within the EX group from baseline to follow-up, 0.8 kg greater ($F(1, 6) = 17.3, p \leq 0.01$, partial $\eta^2 = 0.7$; a medium to large effect size) than the improvement between baseline and week nine. Grip data violated homogeneity of variances and was subsequently transformed. There was no statistically significant difference in the CON group's grip strength between baseline and follow-up.

There was a decrease of 4.0 sec, 95% CI [0.7, 7.1], $p = 0.02$ in the EX group's STS time between baseline (15.2 ± 2.9 sec) and week nine (11.2 ± 2.1 sec). Additionally, there was an improvement in STS time within the EX group between baseline and follow-up, 1.0 sec faster ($F(1, 6) = 18.2, p \leq 0.01$, partial $\eta^2 = 0.8$; a large effect size) than the improvement between baseline and week nine.

There was also an improvement for STS time within the CON group between baseline and follow-up ($F(1, 7) = 5.4, p \leq 0.05$, partial $\eta^2 = 0.4$; a small to medium effect size). The CON group STS time was faster than the EX group at baseline ($F(1, 13) = 6.6, p = 0.02$, partial $\eta^2 = 0.3$; a small to medium effect size) but no significant difference existed at follow-up.

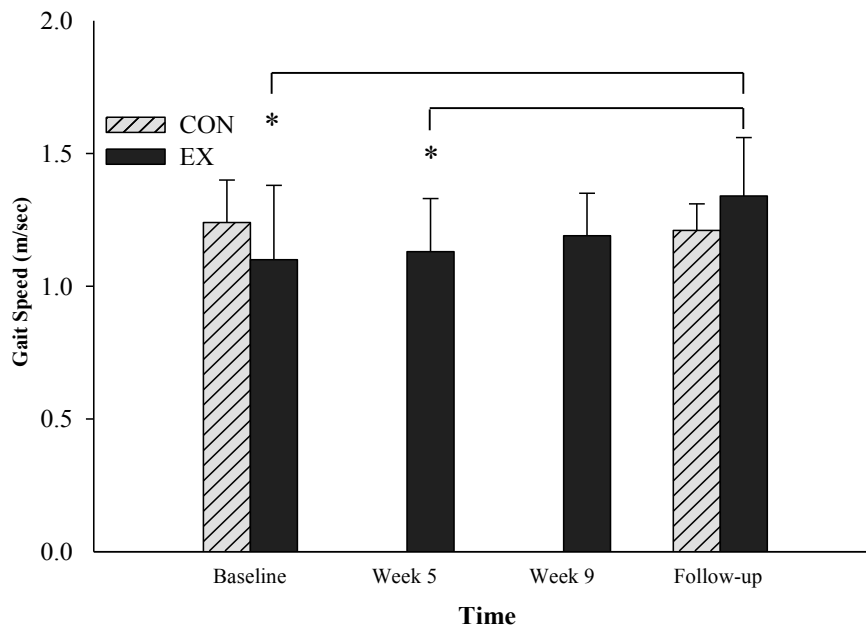


Figure 2.14 Control (CON) and Exercise (EX) group results for gait speed (n = 16) at baseline and follow-up. Intra-group assessments performed on the EX group at week 5 and week 9. m/sec = meters per second; * = significant difference ($p \leq 0.05$) within EX group over time.

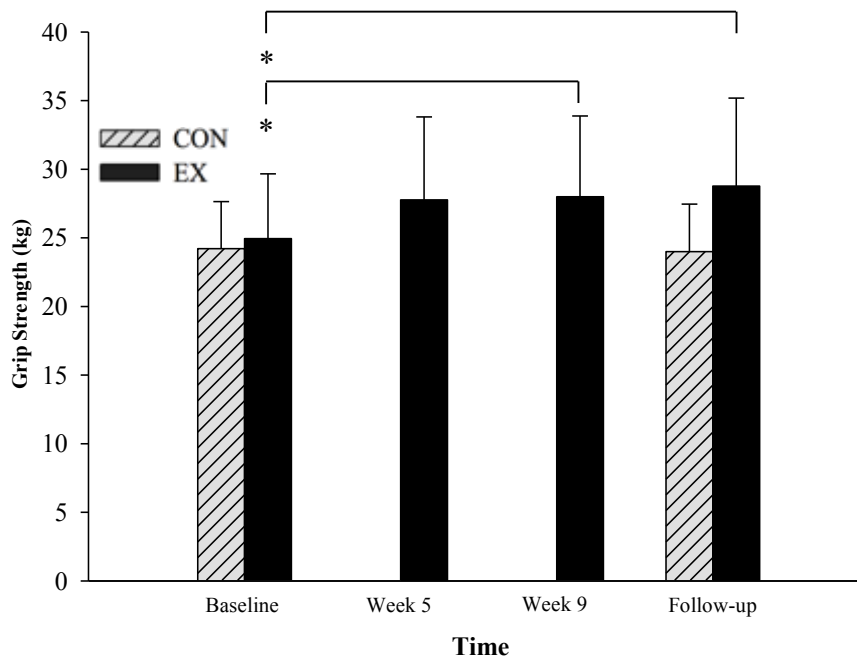


Figure 2.15 Control (CON) and Exercise (EX) group results for grip strength (n = 15) at baseline and follow-up. Intra-group assessments performed on the EX group at week 5 and week 9. kg = kilograms; * = significant difference ($p \leq 0.05$) within EX group over time.

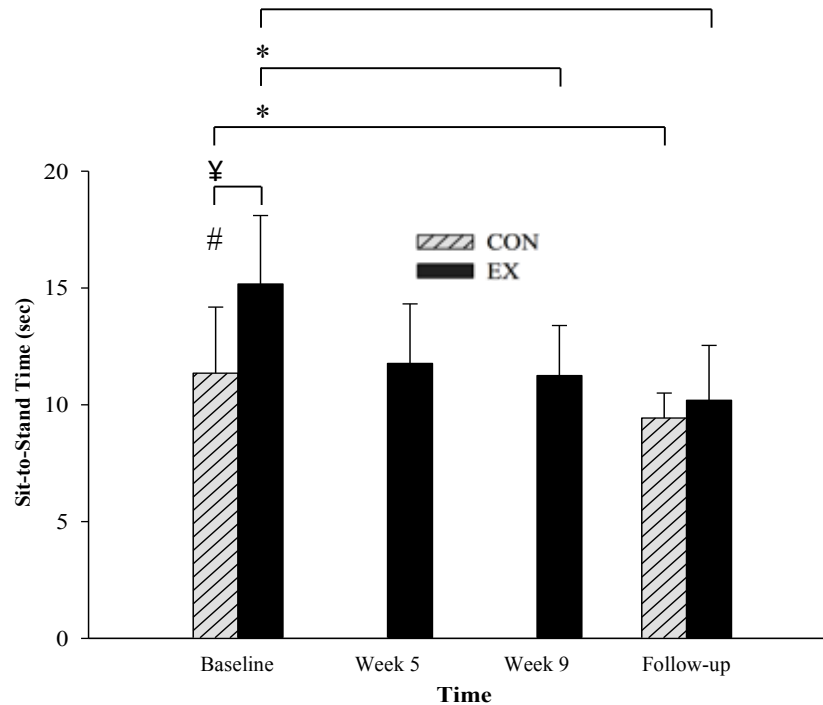


Figure 2.16 Control (CON) and Exercise (EX) group results for sit-to-stand time ($n = 15$) at baseline and follow-up. Intra-group assessments performed on the EX group at week 5 and week 9. sec = seconds; * = significant difference ($p \leq 0.05$) within EX group over time; # = significant difference ($p \leq 0.05$) between CON and EX group; ¥ = significant difference ($p \leq 0.05$) within CON group over time.

Isometric and Isotonic Knee Extension and Elbow Flexion Strength

The results of the KE and EF isometric and isotonic contractions are included in Figures 2.17-2.18. A shoulder injury, unrelated to the exercise program precluded one EX group participant from completing the EF assessments. There was an improvement in KE isometric torque ($F(1, 7) = 5.9, p \leq 0.05$, partial $\eta^2 = 0.5$; a medium effect size) and KE isotonic velocity ($F(1, 7) = 17.5, p \leq 0.01$, partial $\eta^2 = 0.7$; a medium to large effect size) within the EX group from baseline to follow-up. There was also an increase in KE isotonic velocity of 38.2 %/sec, 95% CI [2.0, 74.5], $p = 0.04$ within the EX group between baseline (302.6 ± 40.5 %/sec) and week nine (340.8 ± 36.3 %/sec); 0.7

%/sec faster than the improvement observed between baseline and follow-up. There was no statistically significant difference in the CON group's KE isometric or isotonic strength between baseline and follow-up.

There was a decline in EF isotonic velocity within the CON group from baseline to follow-up ($F(1, 7) = 21.7, p \leq 0.01$, partial $\eta^2 = 0.8$; a large effect size). EF isotonic velocity was faster in the EX group, versus the CON group at follow-up ($F(1, 13) = 4.6, p \leq 0.05$, partial $\eta^2 = 0.3$; a medium to large effect size) but no significant difference existed at baseline.

Correlation

The CON group demonstrated a strong negative correlation between the CFS and KE isometric strength ($r_s = -0.840, p = 0.01$), as well as GS and STS time ($r_s = -0.762, p \leq 0.05$). The CON group also exhibited a strong positive correlation between the CFS and EF isotonic strength ($r_s = 0.708, p = 0.03$). However, only the relationship between the CFS and KE isometric strength was monotonic. The EX group showed a strong positive correlation between the FP and Grip Strength ($r_s = 0.849, p = 0.02$), as well as the CFS and KE isotonic strength ($r_s = 0.748, p = 0.03$) but neither relationship was monotonic (Table 2.2).

Exercise program

All EX group participants progressed each exercise during the intervention. However, calculating a mean group increase in weight lifted or resistance training volume was not possible because some participants only improved ROM and did not progress enough to add resistance; full ROM was required before resistance was added. This occurred with the squat and deadlift exercise. However, Table 2.2.A and Table 2.2.B shows how two participants (participant A and B), who

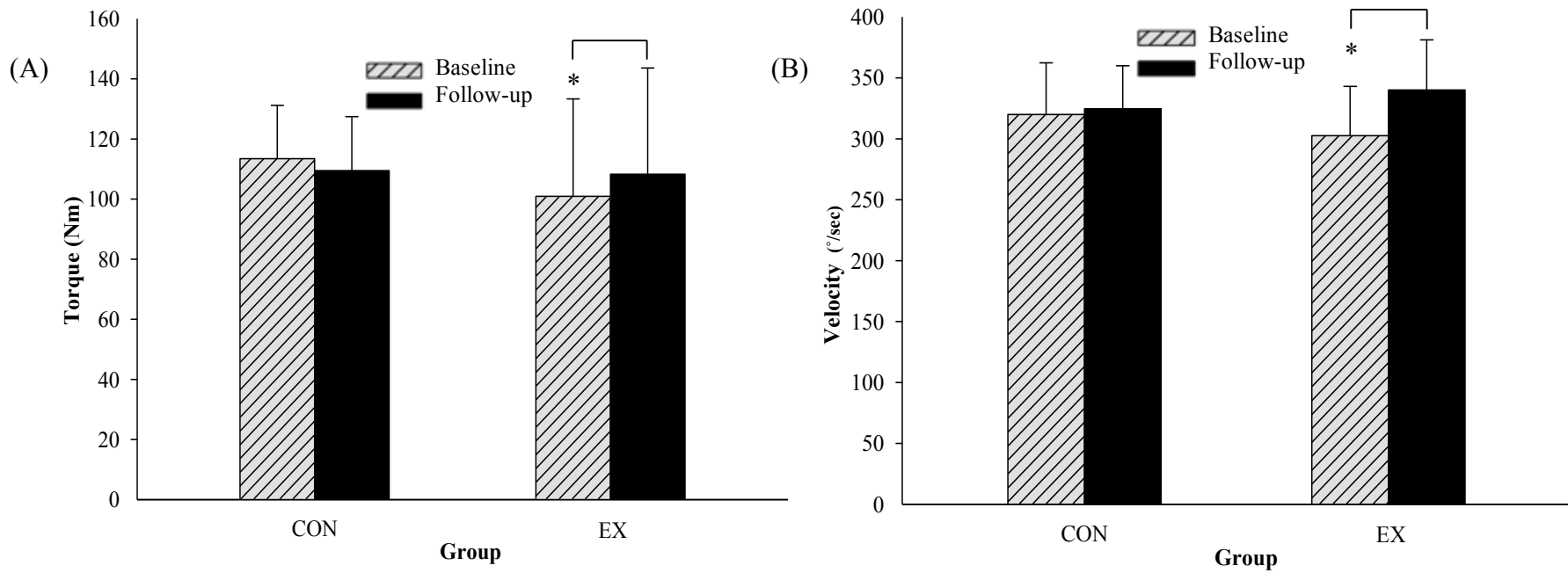


Figure 2.17 Knee extension isometric torque (A) and isotonic velocity (B) for the Control (CON) and Exercise (EX) group (n = 16) at baseline and follow-up. Nm = newton meters; °/sec = degrees per second; * = significant difference ($p \leq 0.05$) within EX group over time.

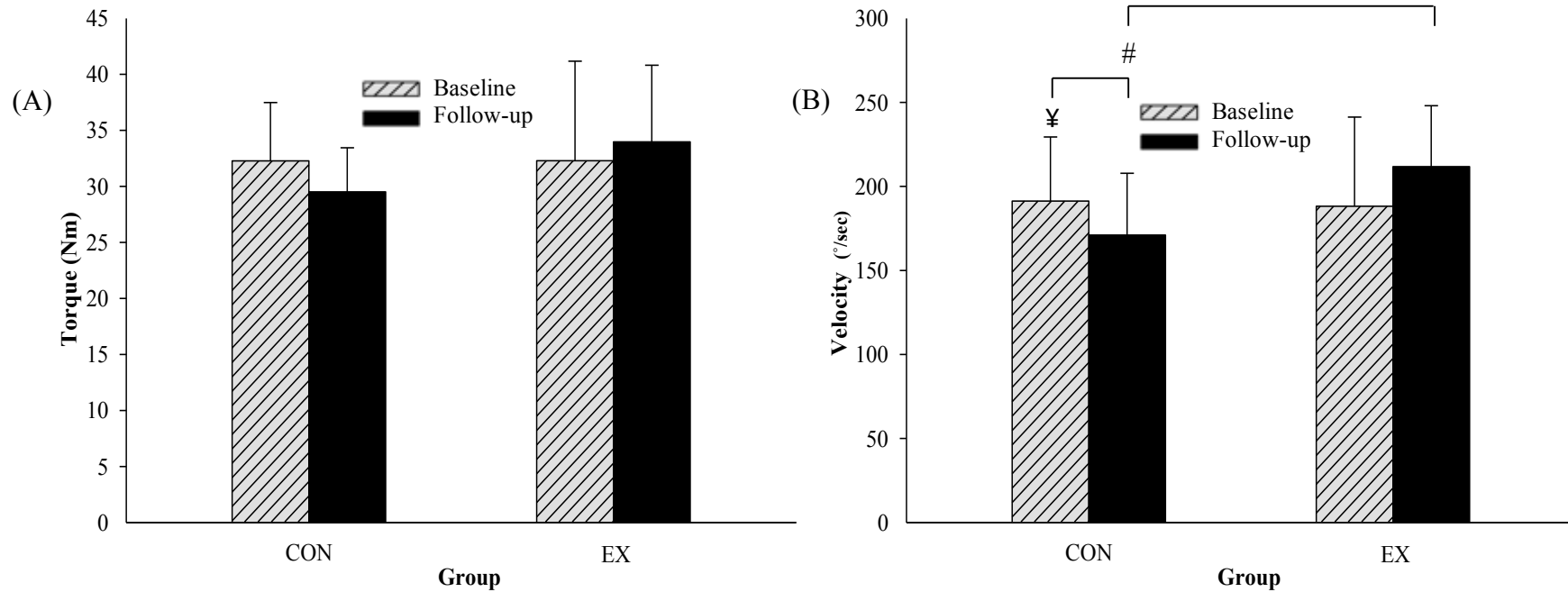


Figure 2.18 Elbow flexion isometric torque (A) and isotonic velocity (B) for the Control (CON) and Exercise (EX) group (n = 15) at baseline and follow-up. Nm = newton meters; °/sec = degrees per second; # = significant difference ($p \leq 0.05$) between CON and EX group; ¥ = significant difference ($p \leq 0.05$) within CON group over time.

Table 2.2 Results of Spearman's rank order correlation between all frailty identification tools and measurement variables.

Frailty Identification Tools	Measurement Variables	CON			EX		
		r_s	p	$\pm \Delta$	r_s	p	$\pm \Delta$
FP $\pm \Delta$ (1-5 units) CON -0.2 EX -0.8	CFS (1-9 units)	0.5	0.2	-0.1	0.6	0.1	-0.5
	GS (m/sec)	0.1	0.8	0	-0.4	0.3	0.2
	Grip Strength (kg)	-0.3	0.5	-0.2	0.8	0.02 *	3.9
	STS Time (sec)	-0.3	0.5	-2.0	0.6	0.2	-5.0
	KE Isometric (Nm)	-0.7	0.1	-3.9	-0.3	0.5	7.4
	KE Isotonic ($^\circ$ /sec)	-0.5	0.3	4.8	0.7	0.1	37.5
	EF Isometric (Nm)	-0.1	0.8	-2.8	-0.3	0.5	1.7
	EF Isotonic ($^\circ$ /sec)	0.3	0.4	-20.2	0.3	0.4	23.6
CFS $\pm \Delta$ (1-9 units) CON -0.1 EX -0.5	GS (m/sec)	-0.4	0.4	0	-0.6	0.1	0.2
	Grip Strength (kg)	-0.4	0.4	-0.2	0.3	0.6	3.9
	STS Time (sec)	0.3	0.5	-2.0	0.5	0.3	-5.0
	KE Isometric (Nm)	-0.8	0.01 *	-3.9	0.2	0.7	7.4
	KE Isotonic ($^\circ$ /sec)	-0.1	0.8	4.8	0.7	0.03 *	37.5
	EF Isometric (Nm)	0.3	0.4	-2.8	0.0	0.9	1.7
	EF Isotonic ($^\circ$ /sec)	0.7	0.05 *	-20.2	0.3	0.5	23.6
GS $\pm \Delta$ (m/sec) CON 0.0 EX +0.2	Grip Strength (kg)	-0.2	0.6	-0.2	-0.3	0.6	3.9
	STS Time (sec)	-0.8	0.03 *	-2.0	-0.3	0.6	-5.0
	KE Isometric (Nm)	0.0	1.0	-3.9	-0.3	0.5	7.4
	KE Isotonic ($^\circ$ /sec)	-0.1	0.8	4.8	-0.6	0.1	37.5
	EF Isometric (Nm)	-0.2	0.7	-2.8	-0.1	0.9	1.7
	EF Isotonic ($^\circ$ /sec)	-0.5	0.2	-20.2	-0.4	0.3	23.6

Note: Table must be interpreted from left to right. FP = Frailty Phenotype; CFS = Clinical Frailty Scale; GS = gait speed; CON = control group; EX = exercise group; r_s = correlation coefficient; $\pm \Delta$ = change between baseline and follow-up; m/sec = meters per second; kg = kilograms; sec = seconds; Nm = newton meters; $^\circ$ /sec = degrees per second; * = $p \leq 0.05$.

performed all four resistance exercises, for the entire program, improved. Each table displays total volume for the week. Volume and intensity (weight resistance) have an inverse relationship; as intensity increases volume decreases and vice versa. Participant “A” could move through a full ROM sooner and therefore, volume increased each week until the last block, where volume reduced to limit the risk of injury. Participant “B” had less strength than participant “A” at week one and as a result, volume continues to increase because of improved ROM.

Table 2.3.A Training progress of participant A.

Exercise	Week			
	1	5	9	12
Squat	2x10x24"	3x10x12"	3x8x35	3x8x45
Bench Press	2x10x35	3x8x45	3x6x50	3x5x55
Deadlift	2x10x18"	3x8x55	3x8x85	3x6x105
Leg Press	2x12x60	3x8x100	3x10x120	3x4x140
Volume (lbs)	2140	4800	7380	5475

Table 2.3.B Training progress of participant B.

Exercise	Week			
	1	5	9	12
Squat	2x12x24"	3x10x18"	3x8x13.5"	3x8x12"
Bench Press	2x8x20	3x8x20	3x8x20	3x5x35
Deadlift	2x10x18"	3x8x12"	3x5x55	3x8x55
Leg Press	2x10x0 *	3x10x0 *	3x10x65	3x8x70
Volume (lbs)	320	480	3255	3525

Note: Each cell represents the number of sets x repetitions x weight. If no resistance was prescribed than box height was used to control ROM. As participants progressed, the box height was lowered until full ROM was achieved and then weights were introduced to the exercise. The last row is total weekly volume calculated as sets x repetitions x weight, cumulative of each exercise. If an

exercise was not performed through a full ROM than it was not included in the weekly volume because the weight value in the calculation would be zero. BW = bodyweight; lbs = pounds; " = inches; * = participant was not moving the lowest possible setting (60lbs) of the leg press through a full range of motion; this had the same effect on volume calculations as other exercises not performed through a full range of motion.

2.4 Discussion

2.4.1 Main Findings

The primary purpose of this investigation was to determine if a MCT exercise program, which emphasized progressive resistance and balance training, would reverse frailty status in pre-frail females. Secondary purposes were to determine if the MCT exercise program would improve; functional task performance, as well as KE and EF isometric and isotonic strength. The first hypothesis was accepted as more participants in the EX group reversed (less frail) and fewer declined (more frail), compared to the CON group. These results provide support for recently published exercise recommendations to reverse frailty (Bray et al., 2016). The second hypothesis was partially accepted. The EX group made significant improvements in functional task performance and measures of strength, while the CON group showed decline in the latter. However, the only significant correlation existed between the CON group's CFS score and KE isometric strength.

Frailty

All EX group participants showed a reversal in frailty status in at least one frailty identification tool. Seventy-five percent of CON group participants showed a decline in frailty status in at least

one frailty identification tool. The EX group FP and CFS score reversed (less frail) by 0.6 and 0.4 more than the CON groups scores, respectively. The FP score in the EX group was very close to non-frail (0.3) at follow-up, reversing from 1.1 at baseline. The CON group received the same follow-up FP score (0.3) but their change was less, based-upon their baseline score of 0.5. EX group CFS score suggested these participants were non-frail (2.9) at follow-up, reversing their frailty status by 0.5 from a baseline score of 3.4. The CON group's CFS score was also non-frail (2.7) at follow-up but this equated to a small change of only 0.1 as baselines scores were 2.8.

According to the FP, CFS and GS, 25, 37.5 and 62.5% more EX group participants showed a reversal (less frail) in frailty status at follow-up, compared to the CON group, respectively. According to the FP, CFS and GS, 12.5, 12.5 and 62.5% more CON group participants showed decline (more frail) in frailty status at follow-up, compared to the EX group, respectively. Only one EX group participant showed decline according to the CFS. However, the degree of decline was negligible (2.5 to 3).

Chan and colleagues (2012) demonstrated that 45% of participants in an exercise and nutrition intervention group reversed their frailty status, versus only 27% of participants in a non-exercise and nutrition group at the 3-month assessment point. However, there was no further significant reversal of frailty scores observed at the six and 12-month assessment points.

Ng and colleagues (2015) demonstrated that the physical exercise and combination groups (physical exercise, nutrition and cognitive training) were the only two interventions to show a significant reversal in frailty status at 3-months, compared to the control group. The exercise group reversed their FP score from 2.2 to 1.2 and the combination group reversed from 2.1 to 1.3. Furthermore, at the 12-month assessment, 35.6-47.8% of all intervention group participants

reversed frailty score, representing a significant reduction, versus only 15% of control group participants.

Post-trial assessments (6-months) by Li and colleagues (2010) revealed that 7.8% of intervention group participants reversed their frailty score, versus 6.4% of control; resulting in a non-significant intervention effect. In all three studies, participants were considered to have reversed frailty if they transitioned from pre-frail to non-frail or frail to pre/non-frail.

Our study reported more (62.5%) EX group participants reversed frailty according to the FP, than Chan (2012), Ng (2015) and Li (2010). However, our study also had more (37.5%) CON group participants reverse frailty status. In comparison to our other frailty identification tools, 75% and 100% of EX group participants reversed frailty status for the CFS and GS, respectively. The number of CON participants that reversed frailty status was consistent between all three tools (37.5%) but it was not the same participants that reported changes.

The heterogeneity in the findings by Chan (2012), Ng (2015) and Li (2012) could be contributed to several factors. Firstly, each intervention used a different frailty tool. Chan and colleagues (2012), as well as Ng and colleagues (2015) utilized modified versions of the FP. Conversely, Li (2010) used the original FP tool. Previous research has identified that modified frailty measurements could affect frailty classification (Dent et al., 2016). These studies included a combination of males and females and did not report frailty status based on sex. Females experience frailty differently than males; they start living with the syndrome earlier but paradoxically live longer (Theou et al., 2014). Therefore, it is possible that females would also experience a reversal in the syndrome differently. Secondly, these studies included a variation of frail and pre-frail participants; recent research has suggested that exercise recommendations should

differ based upon frailty status (Bray et al., 2016). Moreover, a recent systematic review on exercise and frailty excluded those that are pre-frail, citing that they are an entirely different demographic (Gine-Garriga et al., 2014).

To date, only two studies (Kwon et al., 2015; Serra-Prat et al., 2017) have been conducted that focused exclusively on pre-frail participants. Follow-up assessments (12-months) by Serra-Prat and colleagues (2017) revealed that 21.3% of intervention group participants reversed frailty, compared to 15.3% in the control group; however, this difference was not enough to demonstrate statistical significance. Kwon and colleagues (2015) showed a significant improvement in grip strength but this only occurred in the exercise group and it was lost at the follow-up (6-months) assessment.

The lack of significant findings by Serra-Prat (2017) could be that, like other studies (Chan et al., 2012; Li et al., 2010; Ng et al., 2015), these authors included a combination of males and females and did not septate for sex. Kwon et al. (2015) is the only study to use a frailty tool as both an inclusion criteria and outcome measure, and focus exclusively on one frailty demographic (pre-frail) and one sex (female). However, their inclusion criteria assessed only two modified FP indicators. If all five FP indicators were assessed than more participants could have been identified as frail. The modified indicators specified that pre-frail was the lowest quartile, for grip strength and gait speed, of those that attended a “*mass health check-up.*” It is likely that certain individuals were pre-frail and transitioning towards becoming frail, or were already frail and thus, excluded because they were unable to attend the assessment. Therefore, it is possible that the study’s sample size is not a true representation of the population’s lowest quartile for grip strength and gait speed. Finally, their criteria make it impossible to determine the interventions true impact upon frailty

status and thus, compare to other similar studies (Chan et al., 2012, Li et al., 2010, Ng et al., 2015; Serra-Prat et al., 2017).

Functional Performance Tasks

Our study showed a significant improvement in GS (0.24 m/sec) from baseline to follow-up. Ng and colleagues (2015) assessed gait speed and showed a significant improvement in GS in their physical exercise but not the combination intervention group at the three, six and 12-month assessments. Ng and colleagues (2015) assessed gait speed by asking participants to walk “*as fast as possible*” on a 6 m course. They took the average of two trials and reported results in sec and not m/sec. Kwon and colleagues (2015) performed a gait speed test similar to the one performed in our study; participants were instructed to walk at their “*usual*” speed on an 11 m course with a 3 m acceleration and deceleration zone. However, they reported no significant change in gait speed within any group across all time points.

Grip strength is an accurate measure of total body strength (Wind et al., 2010) and poor muscle strength is likely a primary factor that precipitates frailty (Borges et al., 2011). Our study showed a significant improvement in grip strength of 3.1 and 3.9 kg from baseline to week nine and baseline to follow-up, respectively. Kwon and colleagues (2015) also reported a significant improvement in grip strength in their exercise intervention group (2.3 kg \pm 3.1), compared to a control group (0.4 kg \pm 2.6) during the post-intervention assessment (3-months). However, their third intervention group (exercise and nutrition) did not experience similar improvements in grip strength.

Our study was the first to assess STS time in pre-frail older adults, as part of an exercise intervention trial that used a frailty tool as both an inclusion criteria and outcome measure. Sit-to-stand time is indicative of leg strength and time to complete this assessment has been correlated with frailty status (Batista et al., 2012). Our study showed a significant improvement in the EX group's STS time of 4.0 and 5.0 sec from baseline to week nine and baseline to follow-up, respectively. Sit-to-stand time was significantly faster in the CON group at baseline, compared to the EX group. However, there was no significant between-group difference at follow-up. Improvements in functional tasks were similar to those measured in the knee extensors.

Isometric and Isotonic Knee Extension and Elbow Flexion Strength

The EX group showed a significant improvement in KE isometric torque (7.4 Nm) and isotonic velocity (37.5 %/sec) from baseline to follow-up. KE isotonic strength also showed a significant improvement of 38.2 %/sec from baseline to week nine. The CON group demonstrated that a decline (more frail) in frailty status, as measured by the CFS, was associated with a decrease in KE isometric strength.

There were no significant improvements in the EX groups EF isometric or isotonic strength between baseline and any other data collection points. The CON group showed a significant decline in EF isotonic velocity (20.2 %/sec) between baseline and follow-up. This decline made the CON and EX groups significantly different (40.8 %/sec) at follow-up. However, no between-group difference existed at baseline.

The exercise intervention performed in this study incorporated exercises that involved the knee extensor muscles but not the elbow flexors. KE muscles are required to stand-up from the bottom

position of the squat and deadlift, and when returning the inclined leg press sled to the starting position. The bench press requires elbow extension, not flexion, to return the barbell to the starting position. Muscle coactivation is believed to be responsible for the maintenance of the EX group's EF strength; it occurs when there is a synergetic contraction of agonist and antagonist muscles at a surrounding joint (Le et al., 2017). Coactivation of the elbow flexors would have occurred when participants were "*gripping*;" i.e. squatting with weight, bench press, deadlift and holding the handles of the inclined leg press.

The improvements in our EX groups isometric KE values both corroborates and opposes previous research. Only two (Chan et al., 2012; Ng et al., 2015) studies have measured isometric knee extension strength in a pre-frail population. Chan and colleagues (2012) showed significant improvements in the exercise and nutrition group, as well as the non-exercise and nutrition group between baseline and post-intervention (3-months). Therefore, it is unlikely that the exercise was directly responsible for the improvement in isometric knee extension strength. In comparison to a control group, Ng and colleagues (2015) showed a significant improvement in isometric knee extension strength within their cognitive, physical exercise and combination intervention groups. However, this only occurred during the six (post-home exercise period) and 12-month (follow-up) assessments. Reasons for the heterogeneity between the findings of these studies and ours could be that both Chan (2012) and Ng (2015) included pre-frail and frail older adults, as well as males and females. Pre-frail and frail individuals are considered different demographics (Gine-Garriga et al., 2014) and females experience frailty earlier (Theou et al., 2014) and differently (Hubbard et al., 2011) than males. Therefore, reversing the syndrome possibly differs based upon sex. These studies also used different protocols to assess isometric knee extension strength and the data was collected in the field, not under laboratory conditions. Finally, these studies used modified versions

of the FP which could have resulted in misclassification of participant frailty status (Dent et al., 2016).

Our study is the first to identify strength values for isotonic KE, as well as isometric and isotonic EF in pre-frail older adults, as part of an exercise intervention trial that used a frailty tool as both an inclusion criteria and outcome measure. This is interesting considering that muscle weakness is believed to be a major factor in the onset of frailty (Borges et al., 2011).

Exercise Intervention

The exercise intervention was effective and safe for the target population. All EX group participants made progress in resistance and balance training. No EX group participants experienced an adverse event directly related to the exercise program, there were no dropouts and EX group participants completed almost 90% of all exercise sessions. This could be a result of the personal relationships developed between researchers and participants because of the intimate group exercise sessions.

Previous research has identified that variability between exercise interventions studies make it difficult to identify which characteristics of an exercise program are most effective for combating frailty (de Labra et al., 2015; Gine-Garriga et al., 2014; Serra-Prat et al., 2017). However, this exercise program was likely effective at reversing frailty status because of the volume, specificity, intensity and progression of the exercises performed.

Our study performed multiple sets for each exercise. Three previous exercise interventions in pre-frail and frail older adults may have lacked sufficient volume, as participants only performed one set for each exercise (Kwon et al., 2015; Ng et al., 2015; Serra-Prat et al., 2017). The number of

sets performed by the other two exercise interventions is not stated (Chan et al., 2012; Li et al., 2010). Previous research in post-menopausal women considered three sets high-volume (Weisgarber, Candow, & Farthing, 2015).

Previous interventions focused on specific muscle groups for each exercise (Chan et al., 2012; Kwon et al., 2015; Li et al., 2010; Ng et al., 2015); insufficient detail make it unclear if Li and colleagues (2010) focused on specific muscle groups. Conversely, our intervention was comprised of compound movements, which utilized multiple muscle groups at the same time. Furthermore, these compound movements have functional application. For example, the squat replicates standing from a toilet, the bench press carrying or pushing objects, the deadlift picking up an object and the inclined leg press supplements the squat but in a closed-chain circuit. The specificity of these exercises may translate into enhanced performance for activities of daily living and therefore, quality of life. Only Ng and colleagues (2015) reported integrating resistance exercises into functional daily tasks but how this was done was not explained.

Our study utilized high-intensity resistance training. Only one of the five previous studies utilized a repetition range that was conducive to strength accumulation but it only performed one set of two exercises (Kwon et al., 2015). Previous research has highlighted that lower-repetitions with greater intensity (heavier weight) is optimal for increasing strength (Campos et al., 2002; Schoenfeld et al., 2014).

Progressive overload is a necessary principle for creating training adaptations; previous studies (Chan et al., 2012; Kwon et al., 2015; Li et al., 2010; Ng et al., 2015; Serra-Prat et al., 2017) lacked progressive overload via an increase in intensity. Ng and colleagues (2015) stated that intensity increased over the duration of the program; however, it was not clear how this was done.

Additionally, they utilized a repetition range (8-15) not considered optimal for strength accumulation (Campos et al., 2002; Schoenfeld et al., 2014).

This study is the first to assess perceived exertion using an RPE scale, as part of an exercise intervention trial that used a frailty tool as both an inclusion criteria and outcome measure. RPE helped ensure that participants were working at the desired exertion when performing aerobic and resistance training. It also helped supplement researcher's decision-making when progressing resistance training.

In summary, the exercise intervention performed in this study was safe and effective. It utilized high intensity, progressive resistance training in functional, compound movements that utilized dumbbell, barbells and weighted plates. The intensity was confirmed as per RPE and the volume was high in comparison to previous similar studies (Chan et al., 2012; Kwon et al., 2015; Li et al., 2010; Ng et al., 2015; Serra-Prat et al., 2017).

2.4.2 Unique Findings

Progressive Overload

Researchers encouraged participants to overload their muscles by increasing their ROM or number of repetitions or resistance during each training session. However, early in the program it became evident that 6" between box heights was not a small increase in workload for the squat and deadlift exercise. As a result, researchers decided to use bumper plates (ranging in width from ~ 1-3") to make smaller increases in ROM. For example, instead of progressing ROM from an 18" to a 12" box, participants were progressed to 15". What did not work well for progressive overload was assuming all participants would be willing to appropriately overload their resistance training at

each session. Some EX group participants wished to be involved in the decision of how and when they overloaded, rather than follow exercise recommendations. Another interesting finding related to progressive overload is that participants were willing to work at an intensity higher than intended. During the last block of training (weeks 9-12), EX participants regularly reported RPE values > 6 ; this was participant driven and resulted in no adverse effects.

Program Manipulation

All exercises were modified based upon the individual need of the participant. In addition to box height, certain participants placed a 2.5 plate under each heel when performing squats; this helped increase ankle mobility and thus, prevent their heels from lifting off the ground.

The lightest available barbell was 35 lbs. This weight was too heavy for certain participants when performing the bench press, forcing them to use dumbbells that weighed less until they possessed the strength necessary to lift the barbell for the block specific number of sets and repetitions. Unfortunately, the dumbbells increased in 5 lbs increments and thus, made it a challenge to progress participants. For example, progressing from 10 to 15 lbs dumbbells represented a 50% increase. We recommend that future exercise programs possess dumbbells that increase in 2.5 lbs increments.

The inclined leg press exercise also required modification. The weight of the sled (where participants placed their feet while performing the exercise) weighed 60 lbs; this was the lowest possible setting for the exercise. Some participants did not possess the leg strength to press the sled through a full ROM during the early stages of the program. Therefore, participants were instructed to move the sled through a ROM that allowed them to perform the block specific number

of sets and repetitions. Similar to the squat and deadlift, ROM only increased when participants acquired the necessary skill and strength. Resistance weights were added once the participant could press the sled through a full ROM, for the block specific number of sets and repetitions.

Measures of Exercise Intensity

The OMNI-RES was used to quantify RPE after the final set of every resistance training exercise; this tool has been previously validated in an older adult population (Gearhart et al., 2009). The RPE scale was explained to the participants prior to the intervention. Researchers were aware that ratings could be inaccurate during the early stages of the program as previous research has identified that new trainees provide RPE scores that are less accurate than their advanced counterparts (Eston & Williams, 1988; Testa, Noakes, & Desgorces, 2012). However, participants still provided inaccurate ratings well into block two. For, example a participant would give a rating of four “*somewhat easy*” yet be close to muscular failure. Participants also found it difficult to distinguish between the “*middle*” levels (2-9) of the OMNI-RES. This suggests that they could only accurately determine when a set was very easy or very hard. As a result, the RPE method proposed by Zourdos et al., (2016) was utilized from week seven onwards. Using this method, a rating of ten translates to an intensity where the participant cannot perform another repetition. A rating of nine means one repetition remaining and eight means two repetitions remaining. This pattern continues until raters provide a score of 5-6, translating to a range (4-6) of repetitions remaining; a rating \leq four is considered “*light to no*” effort. This RPE scale was easier to understand for participants and provided a more accurate reflection of their exertion.

Group Dynamics

As previously discussed, the EX group was split into two separate groups; morning and afternoon groups. One group appeared to put much more trust in the researchers running the exercise intervention. Additionally, this group approached training with a team mentality, constantly encouraging one another to improve and taking time to recognize certain individuals when they reached a milestone (i.e. starting to squat with weight or deadlift from the ground rather than an elevated box). This group had also become friends outside of the study, creating social events to see one another on non-exercise days or after exercise sessions. Group settings bring together different personalities and it is not realistic to believe that they will consistently exist in harmony. This applies to both the participant-participant and researcher-participant relationship. Group dynamics and its role in exercise interventions is beyond the scope of this study but there is literature dedicated to this field (Beauchamp, & Eys, 2014).

Outside Clinician Influence

Some EX group participants had sought the care of a clinician for an extended period and therefore, relied on the clinician's suggestions rather than the recommendations of the investigator. It became apparent that certain clinicians held negative, preconceived notions towards older females performing high-intensity, progressive resistance training; a common occurrence despite an absence of documented evidence supporting such training methodology leading to injuries (Watson, Weeks, Weis, Horan, & Beck, 2015). As a result, it became difficult to convince some participants to overload or to do so at a faster rate if their clinician held a differing opinion. This effected group dynamics when a participant voiced their clinician's concerns to other group members. Subsequently, this made it more difficult to progress other participants for a brief period.

Chapter 3: Conclusion

3.1 Conclusion

The primary objective of this study was achieved; a MCT exercise intervention, with a focus on resistance and balance training, was able to reverse frailty in pre-frail females within 12-weeks. The exercise program had a positive impact on frailty status, functional task performance, and isometric and isotonic KE and EF strength. The first hypothesis was accepted; in comparison to a CON group, more EX group participants reversed (less frail) and fewer experienced decline (more frail) in their frailty status across all three-frailty identification tools. The second hypothesis was partially accepted as the CON group showed significant correlation between CFS score and KE isometric strength.

3.2 Implications

Our study suggests that MCT, with a focus on resistance and balance training, may be effective at reversing frailty status in pre-frail females. Therefore, the training methodologies used for this intervention could be an effective therapy to reverse frailty. Subsequently, this might help to reduce healthcare costs as frail older adults are considered to be the highest consumers of healthcare resources (Buckinx et al., 2015).

Participants experienced no adverse effects directly related to the exercise intervention. This implies that older females can safely perform high-intensity, progressive resistance training with compound movements that utilize barbells, dumbbells and weighted plates; if the program adheres to the training principle of individuality. These findings support research by Watson and

colleagues (2015), who found a similar style of training to be safe and effective in older females with osteoporosis.

This study also demonstrates that MCT, with a focus on resistance and balance training, can lead to significant improvements in GS, grip strength and STS time. Additionally, such training methods significantly improve KE strength, while maintaining EF strength. Improvement in all of the aforementioned variables may have a positive impact upon quality of life (Brown et al., 2010; Vermeulen et al., 2011).

3.3 Strengths and Limitations

This is the first study to use a validated frailty tool, as both an inclusion criteria and outcome measure, in examining the effectiveness of an exercise intervention in reversing frailty status in pre-frail females. Kwon and colleagues (2015) also focused on pre-frail females but included participants via a modified version of the FP grip strength and gait speed frailty indicators. Therefore, their results should be interpreted with caution (Dent et al., 2016). Similarly, our study is the first to utilize multiple, validated frailty tools, as both an inclusion criteria and outcome measure, in examining the effectiveness of an exercise intervention in reversing frailty status in pre-frail females. Five similar studies have been conducted (Chan et al., 2012; Kwon et al., 2015; Li et al., 2010; Ng et al., 2015; Serra-Prat et al., 2017) but they utilized only one frailty tool. Recent research highlights that a combination of frailty identification tools provides a more reliable measure of frailty, and that the FP and CFS do not always provide the same result (Jones et al., 2016).

This is the first exercise intervention trial that used a frailty tool as both an inclusion criteria and outcome measure, to assess STS time, isotonic KE and EF strength, as well as isometric EF strength. Sit-to-stand time is important as it is indicative of leg strength and time to complete has been correlated with frailty status (Batista et al., 2012). Strength measures provide further insight into the relationship between dynapenia and frailty.

Finally, this is the first exercise intervention trial that used a frailty tool as both an inclusion criteria and outcome measure, to demonstrate a systematic approach to overload when performing high-intensity, progressive resistance training in pre-frail older adults. Previous studies (Chan et al., 2012; Kwon et al., 2015; Li et al., 2010; Ng et al., 2015; Serra-Prat et al., 2017) that focused upon or included a pre-frail population into an exercise intervention, lacked sufficient detail on how exactly participants were progressed.

There were some limitations to this study. Firstly, this study had a small sample size despite beginning with 57 individuals that were interested in the study. Therefore, the study's results should be interpreted with caution. Lack of time was the main reason provided by the 32 participants that declined a baseline assessment; the exercise program took place at a university not centrally located. Future studies should complete an exercise program at a facility that is centrally located and therefore, easy to attend. However, the small group size allowed researchers to know participants on a personal level. This may have positively affected participant's commitment to the program and therefore, explained the high adherence rates and zero dropouts.

Participants were not randomly assigned to the EX or CON groups. Potential participants were very clear that their involvement in the study would be dependent upon their placement into the group of their choosing. Random assignment would have helped to prevent type one error and

thus, ensure that the differences between and within groups were not systematic at the start of the experiment. However, groups only showed a significant difference in STS time at baseline; the CON group was faster but this no longer existed at follow-up. It could also be argued that the EX group was made up of participants who exercised or wanted to exercise but prior exercise participation/interest did not affect health as all participants met the inclusion criteria.

The challenge of identifying frailty is also a limitation in this study. This was expected as the field still lacks a gold-standard for measuring frailty (Sternberg et al., 2011). However, the FP and CFS each possess their own limitations relative to this study. Several participants qualified as pre-frail according to their response to the FP exhaustion questions; this occurred in another similar study (Ng et al., 2015). Previous research has questioned the validity of the FP exhaustion criterion due to significant overlap with depressive traits (Drey et al., 2010). Baseline assessments for this study occurred from early November to late December, a period when the weather starts to become poor in Canada. Follow-up assessments occurred from early March to mid-April, a period when the weather starts to improve. It is possible that the weather affected participant's mood. The change to poor weather during the baseline assessment could have created negative feelings. Conversely, the change to improved weather during the follow-up assessment could have created positive feelings. As a result, participants could have incorrectly qualified as pre-frail and/or showed a reversal in frailty status based upon their response to the exhaustion questions. Previous research has identified the impact of weather on physical activity levels (Jones, Brandon, & Gill, 2017), as well as seasonal depression related-disorders (Rosenthal et al., 1984).

The researcher that conducted the baseline, intra and follow-up assessments was not blinded to the participant's grouping because it was not feasible. The CFS relies upon subjective assessment of

an individual's current health status, to reflect their level of frailty (Theou et al., 2013). It is possible that the researcher was bias towards scoring EX and CON group participants more positively and negatively, respectively. However, the researcher was not aware of the participant's baseline score and one EX group participant still showed decline between baseline and follow-up, according to the CFS.

The total length of the intervention was shorter than recommendations from previous research (Bray et al., 2016). It is possible that a longer intervention could have allowed the CON and EX groups more time to decline/reverse, respectively. This could have led to stronger statistical significance between groups at follow-up. However, 2/3 functional tasks significantly improved by week nine, as well as 1/4 dynamometer measures. Therefore, a shorter intervention could elicit the same response depending on the variables measured. It is unclear if changes in frailty status were correlated with the improvement in functional task performance and KE isotonic strength observed during week nine. Future research should assess frailty status more frequently to determine exactly when changes are occurring.

Recent research highlights that malnutrition overlaps with frailty (Laur et al., 2017), and that a high quality diet is associated better frailty outcomes (Bollwein et al., 2013; Shikany et al., 2014). Similar studies have included a nutrition (Li et al., 2010; Ng et al., 2015), and/or combination (exercise and nutrition) (Chan et al., 2012; Kwon et al., 2015; Li et al., 2010; Ng et al., 2015; Serra-Prat et al., 2017) intervention. Including a diet/nutritional component within our EX group may have facilitated even greater changes, especially in participants who were malnourished but it too was not feasible.

3.4 Future Direction

The findings of this study are positive but a larger clinical trial is required before previous exercise recommendations (Bray et al., 2016) are considered valid. It is imperative that the larger trial still adhere to the same training program and principles outlined within this study. The larger clinical trial should educate all EX group participants on the importance of exercise progression, prior to the start of the intervention. This information session could help both parties obtain a better understanding of the other's goals and concerns.

The inclusion of pre-frail individuals into a larger clinical trial would be easier if a gold-standard frailty identification tool was created. The FP and CFS are the most commonly utilized frailty identification tools (Sternberg et al., 2011) but if the field is to progress then one measure must be accepted as the gold-standard. The creation of a such a tool has never been more needed as Canada (Statistics Canada, 2015) and the world's aging population continues to rise (Cesari et al., 2015). In the absence of a gold-standard tool, it is imperative that researchers continue to use the tools that are available, as both an inclusion criteria and outcome measure, in frailty related studies. The frailty tools that are used must be the original version, as modifications can influence results (Dent et al., 2016) and make it difficult to compare between studies. Research on frailty has grown substantially, publications have increased 82% from 1990-2017 (Drey et al., 2010). However, there are only 15 intervention studies to-date that have used frailty identification tools as both an inclusion criteria and outcome measure (Puts et al., 2017; Serra-Prat et al., 2017). Inclusion of frailty status to screen and assess participant progress will ensure that future studies target their desired population i.e. non-frail, pre-frail or frail and determine if an intervention is effective at

reversing this syndrome. This will allow researchers to identify the characteristics of (exercise) interventions that are most effective at reversing frailty status.

References

- 2017 ICD-10-CM Diagnosis Code R54. (n.d.). Retrieved April 16, 2017, from <http://www.icd10data.com/ICD10CM/Codes/R00-R99/R50-R69/R54-/R54>
- Batista, F. S., Gomes, G. A. de O., Neri, A. L., Guariento, M. E., Cintra, F. A., Sousa, M. da L. R. de, & D'Elboux, M. J. (2012). Relationship between lower-limb muscle strength and frailty among elderly people. *São Paulo Medical Journal = Revista Paulista de Medicina*, 130(2), 102–8. <https://doi.org/10.1590/S1516-31802012000200006>
- Beauchamp, M. R., & Eys, M. A. (2014). *Group dynamics in exercise and sport psychology*. Routledge.
- Bergman, H., Ferrucci, L., Guralnik, J., Hogan, D. B., Hummel, S., Karunanathan, S., & Wolfson, C. (2007). Frailty: an emerging research and clinical paradigm--issues and controversies. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 62(7), 731–7. <https://doi.org/62/7/731> [pii]
- Bollwein, J., Diekmann, R., Kaiser, M. J., Bauer, J. M., Uter, W., Sieber, C. C., & Volkert, D. (2013). Dietary quality is related to frailty in community-dwelling older adults. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, 68(4), 483–489. <https://doi.org/10.1093/gerona/gls204>
- Borg, G. A. (1982). Psychophysical bases of perceived exertion. *Medicine and science in sports and exercise*, 14(5), 377-381. PMID: 7154893
- Borges, L., & Menezes, R. (2011). Definitions and markers of frailty: a systematic review of

literature. *Reviews in Clinical Gerontology*, 21(1), 67–77.
<https://doi.org/10.1017/S0959259810000304>

Bottomley, A. (2002). The Cancer Patient and Quality of Life. *The Oncologist*, 7(2), 120–125.
<https://doi.org/10.1634/theoncologist.7-2-120>

Bray, N. W., Smart, R. R., Jakobi, J. M., & Jones, G. R. (2016). Exercise prescription to reverse frailty. *Applied Physiology, Nutrition, and Metabolism*, 1–5. <https://doi.org/10.1139/apnm-2016-0226>

Brown, N. A., & Zenilman, M. E. (2010). The impact of frailty in the elderly on the outcome of surgery in the aged. *Advances in surgery*, 44(1), 229-249. PMID: 20919524

Buchner, D. M., & Wagner, E. H. (1992). Preventing frail health. *Clinics in geriatric medicine*, 8(1), 1-17. PMID: 1576567

Buchman, A. S., Wilson, R. S., Boyle, P. A., Bienias, J. L., & Bennett, D. A. (2007). Change in motor function and risk of mortality in older persons. *Journal of the American Geriatrics Society*, 55(1), 11–19. <https://doi.org/10.1111/j.1532-5415.2006.01032.x>

Buckinx, F., Rolland, Y., Reginster, J.-Y., Ricour, C., Petermans, J., & Bruyère, O. (2015). Burden of frailty in the elderly population: perspectives for a public health challenge. *Archives of Public Health*, 73(1), 19. <https://doi.org/10.1186/s13690-015-0068-x>

Cadore, E. L., Rodríguez-Mañas, L., Sinclair, A., & Izquierdo, M. (2013). Effects of Different Exercise Interventions on Risk of Falls, Gait Ability, and Balance in Physically Frail Older Adults: A Systematic Review. *Rejuvenation Research*, 16(2), 105–114.

<https://doi.org/10.1089/rej.2012.1397>

- Campos, G. E., Luecke, T. J., Wendeln, H. K., Toma, K., Hagerman, F. C., Murray, T. F., ... & Staron, R. S. (2002). Muscular adaptations in response to three different resistance-training regimens: specificity of repetition maximum training zones. *European Journal of Applied Physiology*, 88(1), 50-60. PMID: 12436270
- Castell, M., Sánchez, M., Julián, R., Queipo, R., Martín, S., & Otero, Á. (2013). Frailty prevalence and slow walking speed in persons age 65 and older: implications for primary care. *BMC Family Practice*, 14, 86. <https://doi.org/10.1186/1471-2296-14-86>
- Cesari, M., Leeuwenburgh, C., Lauretani, F., Onder, G., Bandinelli, S., Maraldi, C., ... Ferrucci, L. (2006). Frailty syndrome and skeletal muscle: Results from the Invecchiare in Chianti study. *American Journal of Clinical Nutrition*, 83(5), 1142–1148. <https://doi.org/10.1037/1528-3542.8.3.425>. Beyond
- Cesari, M., Vellas, B., Hsu, F. C., Newman, A. B., Doss, H., King, A. C., ... Pahor, M. (2015). A physical activity intervention to treat the frailty syndrome in older persons - Results from the LIFE-P study. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, 70(2), 216–222. <https://doi.org/10.1093/gerona/glu099>
- Chan, D. C. D., Tsou, H. H., Yang, R. S., Tsauo, J. Y., Chen, C. Y., Hsiung, C. A., & Kuo, K. N. (2012). A pilot randomized controlled trial to improve geriatric frailty. *BMC Geriatrics*, 12(1), 58. doi: 10.1186/1471-2318-12-58
- Christie, A., Snook, E. M., & Kent-Braun, J. A. (2011). Systematic review and meta-analysis of

skeletal muscle fatigue in old age. *Medicine and Science in Sports and Exercise*, 43(4), 568–577. <https://doi.org/10.1249/MSS.0b013e3181f9b1c4>

Clark, B. C., & Manini, T. M. (2008). Sarcopenia \neq dynapenia. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 63(8), 829–34. <https://doi.org/63/8/829>
[pii]

Collard, R. M., Boter, H., Schoevers, R. A., & Oude Voshaar, R. C. (2012). Prevalence of frailty in community-dwelling older persons: A systematic review. *Journal of the American Geriatrics Society*, 60(8), 1487-1492 <https://doi.org/10.1111/j.1532-5415.2012.04054.x>

Dalton, B. H., Power, G. A., Paturel, J. R., & Rice, C. L. (2015). Older men are more fatigable than young when matched for maximal power and knee extension angular velocity is unconstrained. *Age*, 37(3), 1–16. <https://doi.org/10.1007/s11357-015-9790-0>

Dalton, B. H., Power, G. A., Vandervoort, A. A., & Rice, C. L. (2012). The age-related slowing of voluntary shortening velocity exacerbates power loss during repeated fast knee extensions. *Experimental Gerontology*, 47(1), 85–92. <https://doi.org/10.1016/j.exger.2011.10.010>

Dent, E., Kowal, P., & Hoogendijk, E.O. (2016). Frailty measurement in research and clinical practice: a review. *European Journal of Internal Medicine*. 31, 3–10.

de Labra, C., Guimaraes-Pinheiro, C., Maseda, A., Lorenzo, T., & Millán-Calenti, J. C. (2015). Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials. *BMC Geriatrics*, 15, 154. <https://doi.org/10.1186/s12877-015-0155-4>

- Drey, M., Pfeifer, K., Sieber, C. C., & Bauer, J. M. (2010). The fried frailty criteria as inclusion criteria for a randomized controlled trial: Personal experience and literature review. *Gerontology*, 57(1), 11–18. <https://doi.org/10.1159/000313433>
- Eston, R. G., & Williams, J. G. (1988). Reliability of ratings of perceived effort regulation of exercise intensity. *British Journal of Sports Medicine*, 22(4), 153–5. <https://doi.org/10.1136/bjism.22.4.153>
- Evans, W. J. (1995). What is sarcopenia? *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 50 Spec No, 5–8. https://doi.org/10.1093/gerona/50A.Special_Issue.5
- Felce, D., & Perry, J. (1995). Quality of life: its definition and measurement. *Research in Developmental Disabilities*, 16(1), 51–74. [https://doi.org/10.1016/0891-4222\(94\)00028-8](https://doi.org/10.1016/0891-4222(94)00028-8)
- Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., ... McBurnie, M. A. (2001a). Frailty in Older Adults: Evidence for a Phenotype. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 56(3), M146–M157. <https://doi.org/10.1093/gerona/56.3.M146>
- Fried, L. P., Young, Y., Rubin, G., Bandeen-Roche, K., & WHAS II Collaborative Research Group. (2001b). Self-reported preclinical disability identifies older women with early declines in performance and early disease. *Journal of clinical epidemiology*, 54(9), 889-901. PMID: 11520648
- Gearhart, R. F., Lagally, K. M., Riechman, S. E., Andrews, R. D., Robertson, R. J., Gearhart Jr.,

- R. F., ... Robertson, R. J. (2009). Strength Tracking Using the OMNI Resistance Exercise Scale in Older Men and Women. *Journal of Strength and Conditioning Research*, 23(3), 1011–1015. <https://doi.org/10.1519/JSC.0b013e3181a2ec41>
- Gill, T. M., Gahbauer, E. a, Allore, H. G., & Han, L. (2006). Transitions between frailty states among community-living older persons. *Archives of Internal Medicine*, 166(4), 418–423. <https://doi.org/10.1001/archinte.166.4.418>
- Gine-Garriga, M., Roque-Figuls, M., Coll-Planas, L., Sitja-Rabert, M., & Salva, A. (2014). Physical Exercise Interventions for Improving Performance-Based Measures of Physical Function in Community-Dwelling, Frail Older Adults: A Systematic Review and Meta-Analysis. *Archives of Physical Medicine and Rehabilitation*, 95(4), 753-769. <https://doi.org/10.1016/j.apmr.2013.11.007>
- Gordon, E. H., Peel, N. M., Samanta, M., Theou, O., Howlett, S. E., & Hubbard, R. E. (2016). Sex differences in frailty: a systematic review and meta-analysis. *Experimental Gerontology*, 89, 30-40. PMID:28043934
- Guillemin, F., Bombardier, C., & Beaton, D. (1993). Cross-Cultural Adaptation of Health-Related Quality of Life Measures: Literature Review and Proposed Guidelines. *Journal of Clinical Epidemiology*, 46(12), 1417–1432. [https://doi.org/10.1016/0895-4356\(93\)90142-N](https://doi.org/10.1016/0895-4356(93)90142-N)
- Guralnik, J. M., Simonsick, E. M., Ferrucci, L., Glynn, R. J., Berkman, L. F., Blazer, D. G., ... Wallace, R. B. (1994). A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *Journal of Gerontology*, 49(2), M85-94.

<https://doi.org/10.1093/geronj/49.2.M85>

Hardy, S. E., Perera, S., Roumani, Y. F., Chandler, J. M., & Studenski, S. A. (2007). Improvement in usual gait speed predicts better survival in older adults. *Journal of the American Geriatrics Society*, 55(11), 1727-1734. PMID: 17916121

Hoffman, M., & Payne, V. G. (1995). The effects of proprioceptive ankle disk training on healthy subjects. *The Journal of Orthopaedic and Sports Physical Therapy*, 21(2), 90–93. <https://doi.org/10.2519/jospt.1995.21.2.90>

Hoover, M., Rotermann, M., Sanmartin, C., and Bernier, J. (2013). Validation of an index to estimate the prevalence of frailty among community-dwelling seniors. *Health Reports*, 24(9), 10-17. PMID: 24258362

Hubbard, R. E., & Rockwood, K. (2011). Frailty in older women. *Maturitas*. <https://doi.org/10.1016/j.maturitas.2011.04.006>

Jones, G. R., Brandon, C., & Gill, D. P. (2017). Physical activity levels of community-dwelling older adults are influenced by winter weather variables. *Archives of Gerontology and Geriatrics*, 71, 28–33. <https://doi.org/10.1016/j.archger.2017.02.012>

Jones G.R., Neubauer N., Jakobi J.M. (2016). Physical Activity Predicts Frailty Phenotype. World Congress on Active Aging. *Journal of Aging and Physical Activity*, 24, Suppl., S32.

Klass, M., Baudry, S., & Duchateau, J. (2008). Age-related decline in rate of torque development is accompanied by lower maximal motor unit discharge frequency during fast contractions. *Journal of Applied Physiology*, 104(3), 739–746.

<https://doi.org/10.1152/jappphysiol.00550.2007>

- Kwon J, Yoshida Y, Yoshida H, Kim H, Suzuki T, Lee Y. (2015). Effects of a combined physical training and nutrition intervention on physical performance and health-related quality of life in pre-frail older women living in the community: a randomized controlled trial. *Journal of the American Medical Directors Association*, 16, 263–268. doi: 10.1016/j.jamda.2014.12.005
- Landi, F., Abbatecola, A. M., Provinciali, M., Corsonello, A., Bustacchini, S., Manigrasso, L., ... Lattanzio, F. (2010). Moving against frailty: Does physical activity matter? *Biogerontology*, 11(5), 537-545. <https://doi.org/10.1007/s10522-010-9296-1>
- Lang, P. O., Michel, J. P., & Zekry, D. (2009). Frailty syndrome: A transitional state in a dynamic process. *Gerontology*, 55(5), 539-549. <https://doi.org/10.1159/000211949>
- Lanza, I. R., Towse, T. F., Caldwell, G. E., Wigmore, D. M., & Kent-Braun, J. A. (2003). Effects of age on human muscle torque, velocity, and power in two muscle groups. *Journal of Applied Physiology*, 95(6), 2361–2369. <https://doi.org/10.1152/jappphysiol.00724.2002>
- LaRoche, D. P., Knight, C. A., Dickie, J. L., Lussier, M., & Roy, S. J. (2007). Explosive force and fractionated reaction time in elderly low- and high-active women. *Medicine and Science in Sports and Exercise*, 39(9), 1659–1665. <https://doi.org/10.1249/mss.0b013e318074ccd9>
- Laur, C. V., McNicholl, T., Valaitis, R., & Keller, H. H. (2017). Malnutrition or frailty? Overlap and evidence gaps in the diagnosis and treatment of frailty and malnutrition. *Applied Physiology, Nutrition, and Metabolism*, (999), 1-10. [dx.doi.org/10.1139/apnm-2016-0652](https://doi.org/10.1139/apnm-2016-0652)
- Le, P., Best, T. M., Khan, S. N., Mendel, E., & Marras, W. S. (2017). A review of methods to

assess coactivation in the spine. *Journal of Electromyography and Kinesiology*, 32, 51-60.
<https://doi.org/10.1016/j.jelekin.2016.12.004>

Lee, L., Heckman, G., & Molnar, F. J. (2015). Frailty: Identifying elderly patients at high risk of poor outcomes. *Canadian Family Physician Médecin de Famille Canadien*, 61(3), 227–31.
PMID: 25767167

Lee, L., Patel, T., Costa, A., Bryce, E., Hillier, L. M., Slonim, K., ... & Molnar, F. (2017). Screening for frailty in primary care Accuracy of gait speed and hand-grip strength. *Canadian Family Physician*, 63(1), e51-e57. PMID: 28115460

Levene, H. (1960). Robust tests for equality of variances. *Contributions to probability and statistics*, 1, 278-292.

Li, C.M., Chen, C.Y., Li, C.Y., Wang, W.D., & Wu, S.C. (2010). The effectiveness of a comprehensive geriatric assessment intervention program for frailty in community-dwelling older people: a randomized, controlled trial. *Archives of Gerontology and Geriatrics*, 50, S39–42. doi: 10.1016/S0167-4943(10)70011-X

Liu, C. K., & Fielding, R. A. (2011). Exercise as an Intervention for Frailty. *Clinics in Geriatric Medicine*, 27(1), 101-110. <https://doi.org/10.1016/j.cger.2010.08.001>

Maxwell, S. E., & Delaney, H. D. (2004). *Designing experiments and analyzing data: A model comparison perspective* (Vol. 1). Psychology Press.

Malek-Ahmadi, M., Powell, J. J., Belden, C. M., O'Connor, K., Evans, L., Coon, D. W., & Nieri, W. (2015). Age-and education-adjusted normative data for the Montreal Cognitive

Assessment (MoCA) in older adults age 70–99. *Aging, Neuropsychology, and Cognition*, 22(6), 755-761.

McKinnon, N. B., Montero-Odasso, M., & Doherty, T. J. (2015). Motor unit loss is accompanied by decreased peak muscle power in the lower limb of older adults. *Experimental Gerontology*, 70, 111–118. <https://doi.org/10.1016/j.exger.2015.07.007>

McMillan, G. J., & Hubbard, R. E. (2012). Frailty in older inpatients: What physicians need to know. *Quarterly Journal of Medicine*, 105(11), 1059–1065. <https://doi.org/10.1093/qjmed/hcs125>

Mitnitski, A. B., Mogilner, A. J., & Rockwood, K. (2001). Accumulation of Deficits as a Proxy Measure of Aging. *The Scientific World Journal*, 1, 323–336. <https://doi.org/10.1100/tsw.2001.58>

Mitnitski, A., Song, X., Skoog, I., Broe, G. A., Cox, J. L., Grunfeld, E., & Rockwood, K. (2005). Relative fitness and frailty of elderly men and women in developed countries and their relationship with mortality. *Journal of the American Geriatrics Society*, 53(12), 2184–2189. <https://doi.org/10.1111/j.1532-5415.2005.00506.x>

Moseley, A. M., Lanzarone, S., Bosman, J. M., van Loo, M. a, de Bie, R. a, Hassett, L., & Caplan, B. (2004). Ecological validity of walking speed assessment after traumatic brain injury: a pilot study. *The Journal of Head Trauma Rehabilitation*, 19(4), 341–348. <https://doi.org/10.1097/00001199-200407000-00008>

- Muscedere, J. (2016). Frail seniors: How the healthcare system needs to reorganize to address the needs of some of its most vulnerable clients. *Transforming Canadian Healthcare Through Innovation: The Agenda*, 31.
- Nasreddine, Z. S., Phillips, N. A., Bedirian, V., Charbonneau, S., Whitehead, V., Collin, I., ... Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool for Mild Cognitive Impairment. *Journal of the American Geriatrics Society*, 53(4), 695–699. <https://doi.org/10.1111/j.1532-5415.2005.53221.x>
- Ng, T. P., Feng, L., Nyunt, M. S. Z., Feng, L., Niti, M., Tan, B. Y., ... & Yap, K. B. (2015). Nutritional, physical, cognitive, and combination interventions and frailty reversal among older adults: a randomized controlled trial. *The American Journal of Medicine*, 128(11), 1225-1236. doi: 10.1016/j.amjmed.2015.06.017
- Perera, S., Studenski, S., Chandler, J. M., & Guralnik, J. M. (2005). Magnitude and patterns of decline in health and function in 1 year affect subsequent 5-year survival. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 60(7), 894-900. PMID: 16079214
- Perry, M. C., Carville, S. F., Smith, I. C. H., Rutherford, O. M., & Newham, D. J. (2007). Strength, power output and symmetry of leg muscles: Effect of age and history of falling. *European Journal of Applied Physiology*, 100(5), 553–561. <https://doi.org/10.1007/s00421-006-0247-0>
- Pollock, M. L., Gaesser, G. A., Butcher, J. D., Després, J., Dishman, R. K., Franklin, B. A., & Garber, C. E. (1998). American College of Sports Medicine Position Stand. The

recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Medicine and Science in Sports and Exercise*, 30(6), 975–991. <https://doi.org/10.1097/00005768-199806000-00032>

Puts, M. T. E., Toubasi, S., Andrew, M. K., Ashe, M. C., Ploeg, J., Atkinson, E., ... & McGilton, K. (2017). Interventions to prevent or reduce the level of frailty in community-dwelling older adults: a scoping review of the literature and international policies. *Age and Ageing*, 1-10. PMID: 28064173

Rantanen, T., JM, G., Izmirlian, G., JD, W., EM, S., Ferrucci, L., & LP, F. (1998). Association of muscle strength with maximum walking speed in disabled older women. *American Journal of Physical Medicine & Rehabilitation*, 77(4), 299–305. <https://doi.org/10.1097/00002060-199807000-00008>

Robinson, T. N., Wu, D. S., Stiegmann, G. V., & Moss, M. (2011). Frailty predicts increased hospital and six-month healthcare cost following colorectal surgery in older adults. *American Journal of Surgery*, 202(5), 511–514. <https://doi.org/10.1016/j.amjsurg.2011.06.017>

Rockwood, K., Song, X., MacKnight, C., Bergman, H., Hogan, D. B., McDowell, I., & Mitnitski, A. (2005). A global clinical measure of fitness and frailty in elderly people. *Canadian Medical Association Journal*, 173(5), 489–495. <https://doi.org/10.1503/cmaj.050051>

Roland, K. P., Jakobi, J. M., Powell, C., & Jones, G. R. (2012). Quality of Life As a Determinant of Frailty Phenotype in Community-Dwelling Persons with Parkinson's Disease. *Journal of the American Geriatrics Society*, 60(3), 590-592. doi: 10.1111/j.1532-5415.2011.03862.x

- Roland, K. P., Theou, O., Jakobi, J. M., Swan, L., & Jones, G. R. (2013). How do community Physical and Occupational Therapists Classify Frailty? A pilot Study. *The Journal of Frailty & Aging*, 3(4), 247-250. doi: 10.14283/jfa.2014.32
- Rosenberg, I. H. (1989). Summary comments: epidemiological and methodological problems in determining nutritional status of older persons. *American Journal Clinical Nutrition*, 50, 1231–3. <https://doi.org/10.1007/s13398-014-0173-7.2>
- Rosenberg, I. H. (1997). Sarcopenia: Origins and Clinical Relevance. *Journal of Nutrition*, 127, 990–991. PMID: 9164280
- Rosenthal, N. E., Sack, D. A., Gillin, J. C., Lewy, A. J., Goodwin, F. K., Davenport, Y., ... Wehr, T. A. (1984). Seasonal affective disorder. A description of the syndrome and preliminary findings with light therapy. *Archives of General Psychiatry*, 41(1), 72–80. <https://doi.org/10.1001/archpsyc.1984.01790120076010>
- Schoenfeld, B. J., Ratamess, N. A., Peterson, M. D., Contreras, B., Sonmez, G. T., & Alvar, B. A. (2014). Effects of different volume-equated resistance training loading strategies on muscular adaptations in well-trained men. *The Journal of Strength & Conditioning Research*, 28(10), 2909-2918. PMID: 24714538
- Seco, J., Abecia, L. C., Echevarra, E., Barbero, I., Torres-Unda, J., Rodriguez, V., & Calvo, J. I. (2013). A long-term physical activity training program increases strength and flexibility, and improves balance in older adults. *Rehabilitation Nursing*, 38(1), 37–47. <https://doi.org/10.1002/rmj.64>

- Serra-Prat, M., Sist, X., Domenich, R., Jurado, L., Saiz, A., Roces, A., ... & Papiol, M. (2017). Effectiveness of an intervention to prevent frailty in pre-frail community-dwelling older people consulting in primary care: a randomised controlled trial. *Age and Ageing*. doi: 10.1093/ageing/afw242
- Shikany, J. M., Barrett-Connor, E., Ensrud, K. E., Cawthon, P. M., Lewis, C. E., Dam, T.-T. L., ... Osteoporotic Fractures in Men (MrOS) Research Group. (2014). Macronutrients, diet quality, and frailty in older men. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 69(6), 695–701. <https://doi.org/10.1093/gerona/glt196>
- Statistics Canada. (2015, September 29). Canada's population estimates: Age and sex, July 1, 2015. Retrieved March 14, 2017, from <http://www.statcan.gc.ca/daily-quotidien/150929/dq150929b-eng.htm>
- Statistics Canada. (2016, September 28). Population by sex and age group. Retrieved March 14, 2017, from <http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/demo10a-eng.htm>
- Statistics Canada. (2016, May 19). Life Tables, Canada, Provinces and Territories 2010 to 2012. Retrieved March 14, 2017, from <http://www.statcan.gc.ca/pub/84-537-x/84-537-x2016006-eng.htm>
- Sternberg, S. A., Schwartz, A. W., Karunanathan, S., Bergman, H., & Mark Clarfield, A. (2011). The identification of frailty: A systematic literature review. *Journal of the American Geriatrics Society*, 59(11), 2129-2138. <https://doi.org/10.1111/j.1532-5415.2011.03597.x>
- Sweet, T. W., Foster, C., McGuigan, M. R., & Brice, G. (2004). Quantitation of resistance training

- using the session rating of perceived exertion method. *Journal of Strength and Conditioning Research*, 18(4), 796–802. <https://doi.org/10.1519/14153.1>
- Tabachnick, B. G., Fidell, L. S., & Osterlind, S. J. (2001). Using multivariate statistics.
- Testa, M., Noakes, T. D., & Desgorces, F.D. (2012). Training state improves the relationship between rating of perceived exertion and relative exercise volume during resistance exercises. *Journal of Strength and Conditioning Research / National Strength & Conditioning Association*, 26(11), 2990–2996. <https://doi.org/10.1519/JSC.0b013e31824301d1>
- Tewfik, G. I. (1953). Suxamethonium-modified electroconvulsive therapy in the frail and elderly. *The Lancet*, 262(6777), 110-112. PMID: 13070551
- Theou, O., Brothers, T. D., Mitnitski, A., & Rockwood, K. (2013). Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. *Journal of the American Geriatrics Society*, 61(9), 1537–1551. <https://doi.org/10.1111/jgs.12420>
- Theou, O., Brothers, T. D., Peña, F. G., Mitnitski, A., & Rockwood, K. (2014). Identifying common characteristics of frailty across seven scales. *Journal of the American Geriatrics Society*, 62(5), 901–906. <https://doi.org/10.1111/jgs.12773>
- Theou, O., Stathokostas, L., Roland, K. P., Jakobi, J. M., Patterson, C., Vandervoort, A. A., & Jones, G. R. (2011). The effectiveness of exercise interventions for the management of frailty: a systematic review. *Journal of Aging Research*. <https://doi.org/10.4061/2011/569194>
- Thode, H. C. (2002). *Testing for normality* (Vol. 164). CRC press.

- Tieland, M., van de Rest, O., Dirks, M. L., van der Zwaluw, N., Mensink, M., van Loon, L. J. C., & de Groot, L. C. P. G. M. (2012). Protein Supplementation Improves Physical Performance in Frail Elderly People: A Randomized, Double-Blind, Placebo-Controlled Trial. *Journal of the American Medical Directors Association*, 13(8), 720–726. <https://doi.org/10.1016/j.jamda.2012.07.005>
- Van Kan, G. A., Rolland, Y., Bergman, H., Morley, J. E., Kritchevsky, S. B., & Vellas, B. (2008a). The IANA Task Force on frailty assessment of older people in clinical practice. *Journal of Nutrition, Health and Aging*, 12(1), 29-37. PMID: 18165842
- Van Kan, G. A., Rolland, Y., Bergman, H., Morley, J. E., Kritchevsky, S. B., Vellas, B., & Panel, G. A. (2008b). Frailty assessment of older people in clinical practice expert opinion of a geriatric advisory panel. *Journal of Nutrition, Health and Aging*, 12(1), 29-38. PMID: 18165842
- Van Kan, G. A., Rolland, Y., Andrieu, S., Bauer, J., Beauchet, O., Bonnefoy, M., ... & Nourhashemi, F. (2009). Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an International Academy on Nutrition and Aging (IANA) Task Force. *Journal of Nutrition, Health and Aging*, 13(10), 881-889. PMID: 19924348
- Veale, J. F. (2014). Edinburgh Handedness Inventory Á Short Form: A revised version based on confirmatory factor analysis. *Laterality*, 19(2), 164–177. <https://doi.org/10.1080/1357650X.2013.783045>
- Vermeulen, J., Neyens, J. C. L., van Rossum, E., Spreuwenberg, M. D., & de Witte, L. P. (2011). Predicting ADL disability in community-dwelling elderly people using physical frailty

indicators: a systematic review. *BMC Geriatrics*, 11(1), 33. <https://doi.org/10.1186/1471-2318-11-33>

Walston, J., Hadley, E. C., Ferrucci, L., Guralnik, J. M., Newman, A. B., Studenski, S. a, ... Fried, L. P. (2006). Research agenda for frailty in older adults: toward a better understanding of physiology and etiology. *Journal of the American Geriatrics Society*, 54, 991–1001. <https://doi.org/10.1111/j.1532-5415.2006.00745.x>

Warburton, D. E. R., Bredin, S. S. D., Jamnik, V. K., & Gledhill, N. (2011). Validation of the PAR-Q+ and ePARmed-X+. *The Health & Fitness Journal of Canada*, 4(2), 38-46

Watson, S. L., Weeks, B. K., Weis, L. J., Horan, S. A., & Beck, B. R. (2015). Heavy resistance training is safe and improves bone, function, and stature in postmenopausal women with low to very low bone mass: novel early findings from the LIFTMOR trial. *Osteoporosis International*, 26(12), 2889–2894. <https://doi.org/10.1007/s00198-015-3263-2>

Watt, J. R., Jackson, K., Franz, J. R., Dicharry, J., Evans, J., & Kerrigan, D. C. (2011). Effect of a supervised hip flexor stretching program on gait in frail elderly patients. *American Journal of Physical Medicine & Rehabilitation*, 3(4), 330-335. PMID: 21497319

Weisgarber, K. D., Candow, D. G., & Farthing, J. P. (2015). Whey protein and high-volume resistance training in postmenopausal women. *Journal of Nutrition, Health and Aging*, 19(5), 511–517. <https://doi.org/10.1007/s12603-015-0454-7>

Wind, A. E., Takken, T., Helders, P. J. M., & Engelbert, R. H. H. (2010). Is grip strength a predictor for total muscle strength in healthy children, adolescents, and young adults? *European*

Journal of Pediatrics, 169(3), 281–287. <https://doi.org/10.1007/s00431-009-1010-4>

Xue, Q. L. (2011). The Frailty Syndrome: Definition and Natural History. *Clinics in Geriatric Medicine*, 27(1), 1-15. <https://doi.org/10.1016/j.cger.2010.08.009>

Yoon, T., Doyel, R., Widule, C., & Hunter, S. K. (2015). Sex differences with aging in the fatigability of dynamic contractions. *Experimental Gerontology*, 70, 1–10. <https://doi.org/10.1016/j.exger.2015.07.001>

Yoon, T., Schlinder-Delap, B., & Hunter, S. K. (2013). Fatigability and recovery of arm muscles with advanced age for dynamic and isometric contractions. *Experimental Gerontology*, 48(2), 259–268. <https://doi.org/10.1016/j.exger.2012.10.006>

Zourdos, M. C., Klemp, A., Dolan, C., Quiles, J. M., Schau, K. A., Jo, E., ... & Blanco, R. (2016). Novel Resistance Training–Specific Rating of Perceived Exertion Scale Measuring Repetitions in Reserve. *The Journal of Strength & Conditioning Research*, 30(1), 267-275. PMID: 26049792

Appendices

Appendix A: Ethics Approval



The University of British Columbia
Office of Research Ethics
Clinical Research Ethics Board – Room 210, 828 West
10th Avenue, Vancouver, BC V5Z 1L8

ETHICS CERTIFICATE OF FULL BOARD APPROVAL

PRINCIPAL INVESTIGATOR: Gareth R. Jones	INSTITUTION / DEPARTMENT: UBC/UBCO Health & Social Development/UBCO Health and Exercise Sciences	UBC CREB NUMBER: H16-00712
INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:		
Institution		Site
UBC		Okanagan
Other locations where the research will be conducted: N/A		
CO-INVESTIGATOR(S): Nicholas Bray Jennifer M. Jakobi		
SPONSORING AGENCIES: N/A		
PROJECT TITLE: A Multi-Component Exercise Intervention for Pre-Frail Older Females.		
THE CURRENT UBC CREB APPROVAL FOR THIS STUDY EXPIRES: October 11, 2017		
<p>The full UBC Clinical Research Ethics Board has reviewed the above described research project, including associated documentation noted below, and finds the research project acceptable on ethical grounds for research involving human subjects and hereby grants approval.</p> <p>This approval applies to research ethics issues only. The approval does not obligate an institution or any of its departments to proceed with activation of the study. The Principal Investigator for the study is responsible for identifying and ensuring that resource impacts from this study on any institution are properly negotiated, and that other institutional policies are followed. The REB assumes that investigators and the coordinating office of all trials continuously review new information for findings that indicate a change should be made to the protocol, consent documents or conduct of the trial and that such changes will be brought to the attention of the REB in a timely manner.</p>		
REB FULL BOARD MEETING REVIEW DATE: October 11, 2016		
DOCUMENTS INCLUDED IN THIS APPROVAL:		DATE DOCUMENTS APPROVED:
Document Name	Version	Date
Protocol:		
Research Proposal	Ver. 3.0	November 2, 2016
Consent Forms:		
Letter of Information and Consent Form	Ver. 4.0	November 3, 2016
Advertisements:		
Newspaper / Social Network Ad	Version 2.0	October 25, 2016
Brochure	Version	October 25,
		November 3, 2016

Appendix B: Clinical Trials Registration

Protocol Registration and Results System (Logo)

ID: H16-00712

Exercise Intervention to Reverse Frailty

NCT02952443

Protocol Registration Preview

Exercise Intervention to Reverse Frailty (ERF)

*This study is not yet open for participant recruitment.
Verified October 2016 by Gareth Jones, University of British Columbia*

Sponsor:
University of British Columbia

Information provided by (Responsible Party):
Gareth Jones, University of British Columbia

ClinicalTrials.gov Identifier:
NCT02952443

First received: October 31, 2016
Last updated: November 1, 2016
Last verified: October 2016

Purpose

The objective of this study is to evaluate a multi-component exercise intervention as an effective therapy to reverse pre-frailty phenotype in females age 65 or older. Participants will be screened for frailty phenotype using the Cardiac Health Study - Frailty Index (CHS); the Clinical Frailty Scale (CFS); and a measure of self-paced normal walking speed. Participants undergo baseline evaluation to determine frailty phenotype and then those females who meet the pre-frailty criteria are randomized into one of two groups; 1) Multi-component exercise program, or 2) A control group who receives a monthly newsletter on tips for successful aging. The exercise group will participate in multi-component exercise program which will emphasize resistance training but also include aerobic, balance and flexibility components 3 times a week at 45 to 60 minutes/session for 16 consecutive weeks. The control group will be asked to maintain normal daily-living habits for the duration of the 16-week study.

Condition	Intervention
Fragility	Behavioral: Exercise Behavioral: Control

Appendix C: Leg Dominance Questions

Leg Dominance Questions:

1. What leg did they lead with when stepping onto the force platform: Left or Right
2. What leg do they stand on for a one legged balance test: Left or Right
3. What did they respond with when asked which is their dominant leg: Left or Right
4. What is their self-selected dominant leg: Left or Right
5. What leg would you use to kick a soccer ball: Left or Right
6. Do they have or have they had any major injuries to either leg: Yes or No

a. Notes about Injuries:

Appendix D: Recording Sheet for Dynamometer Settings

Participant Name: _____

Dynamometer Settings				
		Leg		Arm
Dominant Arm		x		
Dominant Leg				
Chair Front/Back				
Chair Height				
Chair Rotation				
Dynamometer Left/Right				
Dynamometer Height				
Dynamometer Tilt				
Dynamometer Rotation				
Attachment Length				

		Leg		Arm	
Seat Back Fore/Aft.					
Seat Tilt					
Distance to Dynamometer					
Limb Support		X			
Shoulder Abduction		X			
Shoulder Flexion		X			
Elbow Flexion/Extension		X			
Dynamometer Position					
Hip Flexion					

Appendix E: Training Equipment



- Custom made wooden boxes
 - Two - 12" high x 18 wide x 24 long
 - Six - 6" high x 18 wide x 24 long
- Progression Dumbbells, 5 – 45lbs, Progression Fitness Equipment, Saskatoon, SK
- Progression Bumper Plates, 10, 25 and 45lbs, Progression Fitness Equipment, Saskatoon, SK
- X-Plode 250 Half Cage (PFX-250), Progression Fitness Equipment, Saskatoon, SK
- FreeMotion 250u Exercise Bike, FreeMotion Fitness, Logan, UT
- Star Trac Pro Treadmill, Core Health and Fitness, Vancouver, WA
- ProForm 1280s Elliptical Interactive Trainer, ProForm, Logan, UT
- Freespirit Elliptical 903, Spirit Fitness, Jonesboro, AR
- Marcy Bench Rack MD-859P, MARCY Pro, Pomona, California
- Bowflex 3.1 Adjustable Bench, Nautilus Incorporated, Vancouver, WA
- TuffStuff PPL-960 45° Leg Press, TuffStuff Fitness Equipment, Chino, CA
- No name weight plates
- No name barbells

Appendix F: Exercise Progressions for Resistance and Balance Training

Resistance Training			
Squat	Deadlift	Flat Bench Press	Leg Press
Bodyweight (BW) to 30" box, progressing down to 12" box	35lbs barbell from 30" box, progressing down to 12" box	Dumbbells	Sled to as low as possible without pain and proper form
		35lbs barbell	
Goblet squat to 12" box	45lbs barbell from 12" box	45lbs barbell	Sled through full range of motion
	From ground		Sled plus weight
Static Balance Training			
Side-by-side	Semi-Tandem	Tandem	Balance On One Leg
		Eyes Closed	Touch nose
			Eyes closed
			Touch nose with eyes closed
Dynamic Balance Training			
Weight Shifts	Step Overs	Walking a Line	
	Small dumbbell (5-15lbs) on side	Double the distance	
		Large dumbbell (20-35lbs) on side	Double the distance, arms extended straight overhead, palms touching
	Small dumbbell (5-15lbs) stood upright		
	Large dumbbell (20-35lbs) stood upright		

Note: Balance training exercises progress in difficulty from left to right, and within an exercise from top to bottom.

Appendix G: Training Log Sheet Used by Participants

	PARTICIPANT ID:				WEEK	DATE									
DAY 1					DAY 2					DAY 3					
AEROBIC															
EQUIP	TIME	5	10		EQUIP	TIME	5	10		EQUIP	TIME	5	10		
	RPE					RPE					RPE				
RESISTANCE															
EXERCISE	SETS	REPS	WT	RPE	NOTES	SETS	REPS	WT	RPE	NOTES	SETS	REPS	WT	RPE	NOTES
SQUAT															
DEADLIFT															
BENCH PRESS															
LEG PRESS															
BALANCE															
EXERCISE	SETS	REPS/TIME	NOTES	EXERCISE	SETS	REPS	NOTES	EXERCISE	SETS	REPS	NOTES				
FLEXIBILITY															
EXERCISE	SETS	REPS/TIME	NOTES	SETS	REPS/TIME	NOTES	SETS	REPS/TIME	NOTES						
HIP FLEXOR															