4-11-2010 12:00 AM

Physical Function During Performance-Based Tasks and Throughout Daily Life. Is It Different Across Levels of Frailty?

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A thesis submitted in partial fulfillment of the requirements for the degree in Doctor of Philosophy

PHYSICAL FUNCTION DURING PERFORMANCE-BASED TASKS AND THROUGHOUT DAILY LIFE. IS IT DIFFERENT ACROSS LEVELS OF FRAILTY?

(Spine title: Physical Function Across Levels of Frailty)

(Thesis format: Integrated-Article)

by

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of the requirements for the degree of
Doctor of Philosophy

The School of Graduate and Postdoctoral Studies
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London, Ontario, Canada

THE UNIVERSITY OF WESTERN ONTARIO
SCHOOL OF GRADUATE AND POSTDOCTORAL STUDIES

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The thesis by

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Date______________________________

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Chair of the Thesis Examination Board

Abstract

The overall aim of this thesis was to provide a more focused understanding about the physical function of older women across levels of frailty. The specific aims were: 1) Examine the physical function of older women across levels of frailty during performance-based tasks and throughout their normal daily life; and 2) Review the effectiveness of current exercise interventions for the management of frailty. To answer these aims an observational study of community-dwelling older women (63-100 years) from rural Greece and a comprehensive systematic review on the impact of exercise on frail older adults were conducted.

The performance-based measures that had the strongest association with frailty were ambulatory mobility, lower body muscular endurance, and non-dominant handgrip strength. Walking at a preferred pace was more related to frailty than walking at maximal pace and grip strength of the non-dominant hand had a stronger association with frailty compared to the dominant hand. In addition, accelerometers showed good agreement with the other physical activity tools, had the strongest association with frailty, and could be used to dissociate levels of frailty. This thesis showed that multiple methods can be used to accurately determine the duration and intensity of physical activity in older adults across levels of frailty since each method examined in this thesis had limitations but provided useful information about different aspects of physical activity. Muscle activity and quiescence, as measured with portable electromyography, may add insight to the dissociation of frailty since they differ across levels of frailty and may also be used to indicate differences between the upper and lower body muscles. Finally, the systematic review indicated that structured exercise training can have a positive effect on frail older adults and thus can be helpful for the management of frailty. Multicomponent training interventions, of long duration (≥ 5 months), performed three times per week, for 30-45 minutes per session, generally had superior outcomes than other exercise programs. The findings from this thesis indicated that the criteria selected to define frailty and the measurement protocols for these criteria are important. Future investigations will help classify the potential role of these measures in preventing further functional decline.

Keywords: frail, levels of frailty, aging, older adults, community-dwelling, women, physical function, physical activity, mobility, accelerometer, global positioning system, heart rate, electromyography, exercise

Co-Authorship

This thesis contains materials from four manuscripts (Chapters 2-5). Three manuscripts are currently under peer-review in notable scientific journals for this field of research (Chapters 2,4,5) and one manuscript is in final preparation (Chapter 3):

- Theou O, Jones GR, Jakobi JM, Mitnitski A, Vandervoort AA. Relationship between Frailty and Physical Function Performance-based Measures. J Am Geriatr Soc (submitted April, 2010)
- Theou O, Jones GR, Jakobi JM, Vandervoort AA. A Comparison of Physical Activity Tools in Older Women Across Levels of Frailty. (in preparation)
- Theou O, Jakobi JM, Vandervoort AA., Jones GR. Daily Muscle Activity and Quiescence in Non-Frail, Pre-Frail, and Frail Older Women. Exp Gerontol (accepted August, 2010)
- Theou O, Stathokostas L, Roland K, Jakobi JM, Patterson C, Vandervoort AA., Jones GR. The Effectiveness of Exercise Interventions for the Management of Frailty: A Systematic Review. Can J Aging (submitted November, 2009)

The first author on all manuscripts was O. Theou who collected, analyzed, and interpreted the data of this thesis and wrote the manuscripts. In addition to O. Theou, all manuscripts were co-authored by GR. Jones, JM. Jakobi, and AA. Vandervoort who provided ongoing feedback to O. Theou during the design and implementation of these studies and the writing of the manuscripts. Chapter 2 had an additional co-author, A. Mitnitski, who assisted on the data analysis for this study. Chapter 5 was co-authored by L. Stathokostas who assisted with the design and acted as a reviewer, K. Roland who acted as a reviewer, and C. Patterson who helped with the conceptualization of the study.

Acknowledgments

This thesis would not have been completed without the guidance and support of many people who made the last four years an exceptional experience. First, I would like to thank my co-supervisors Dr. Gareth Jones and Dr. Tony Vandervoort. You were incredible mentors who not only play a major role in this thesis but also assisted me in becoming an independent researcher. I cannot express my appreciation for always making time to meet and being so patient with me. Our long multi-topic discussions will definitely be valuable for my future career. I was very fortunate to have a third mentor, Dr. Jennifer Jakobi, who shared her passion for basic science physiology allowing me to move beyond my applied research background. Thank you for being there during stressful moments at work and helping me complete this thesis on time. Tony, Gareth, and Jenn thank you for making Canada feel like home.

Next I would like to acknowledge the positive influence that the Health and Rehabilitation Sciences program had on me during my thesis. My interaction with the faculty, Dr. Aleksandra Zecevic, Dr. Tom Overend, Dr. Marita Kloseck, Dr. Debbie Rudman, and Dr. Dorothy Forbes challenged me to think critically from all aspects of quantitative and qualitative research. I am also grateful to the Faculty of Graduate Studies and Health Sciences at the University of Western Ontario and other funding agencies (CIHR, NICE, BCNAR) for their financial support throughout my candidacy. Further I would like to thank Dr. Lisa Stathokostas and my friends and colleagues in the Human Kinetics lab at UBCO for keeping me motivated, listening to my complaints, and accepting my cultural differences. I will never forget the fun we had during our social meetings.

I would like to express my gratitude to the older women who participated in my studies and the participants at my exercise classes at the Canadian Center for Activity and Aging. Our interaction gave me an appreciation for the beauty of aging. Finally, I would like to thank my family and friends in Greece. To my parents thank you for believing in my abilities and teaching me that nothing is impossible. To my brother thank you for showing me the importance of enjoying work. To my Greek friends thank you for staying close to me regardless of the long distance and for being there when I needed you. Most importantly I would like to thank my grandparents. I was fortunate to grow up with three exceptional people whose goal in life was/has been to die young in heart as late as possible.

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List of Abbreviations

ADL	activities of daily living
ACSM	American College of Sports Medicine
ANOVA	analysis of variance
BADL	basic activities of daily living
BB	biceps brachii
BF	biceps femoris
BMI	body mass index
EMG	electromyography
FI	Frailty Index
GV	gait velocity
GPS	global positioning systems
HR	heart rate
HRR	heart rate reserve
IADL	instrumental activities of daily living
IGF-I	insulin-like growth factor-I
KE	knee extension
LTC	long-term care facilities
VO_2max	maximal oxygen consumption
MVE	maximal voluntary exertions
SF-36	Medical Outcomes Survey Short-Form 36
MET	metabolic equivalent
MLTAQ	Minnesota Leisure Time Activity Questionnaire

1RM	one repetition maximum
PA	physical activity
SL	stride length
TB	triceps brachii
VL	vastus lateralis

CHAPTER 1

Introduction and Background[a]

1.1 Frailty

In almost every country throughout the world, the proportion of older adults, those 65+ years of age, is growing faster than any other age group. In Canada the number of older adults is expected to double to ~ 8.6 million within the next 25 years.[1] Although the majority of older adults consider themselves to be in good health and lead independent lives, 91% have one or more chronic conditions, 40% live with a disability[2] and a considerable proportion (10-25%) are considered frail.[3] The number of frail older individuals is expected to grow substantially in the very near future.

The knowledge-base related to understanding frailty has increased exponentially within the past decade.[4,5] While frailty is increasingly recognized as a geriatric syndrome[b],[6,7] the terms "frail" and "frailty" are often used in the literature without a clear definition or criteria. Frailty's precise definition and mechanisms continue to be matters of debate.[8] There is an urgent need for agreement on a definition of frailty among health care professionals to optimize the identification and treatment of frail individuals.[9]

A variety of theoretical definitions exists. Some focus on the presence of dependency while others emphasize disease state.[10] For example, Hamerman[11] defined frailty as the midpoint between independence[c] and pre-death. The current understanding is that frailty is a result of cumulative multisystem deterioration and represents a loss in

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[a] Sections reprinted from published articles in "Physical and Occupational Therapy in Geriatrics" (Appendix G.1a) and "Applied Physiology Nutrition and Metabolism" (Appendix G.1b) Journals with permission from the publisher

[b] Multifactorial health conditions (e.g. pressure ulcers, falls, incontinence, delirium) that occur when the accumulated effects of impairments in multiple systems render an older person vulnerable to situational challenges

[c] Fully functional with activities of daily living and instrumental activities of daily living

one's reserve capacity[a] below a level to sustain homeostasis required to meet the demands of everyday life.[12] Frail older adults are vulnerable to physiological and psychological stressors, and are at risk for a range of adverse health events such as falls, fractures, subsequent disability, and death. Such adverse health events place a substantial financial strain upon health care resources.[10,13,14] Although, frailty is often associated with institutional care,[15] the majority of frail older adults actually live in the community[16,17] despite some degree of impairment in one or more activities of daily living (ADL).

Frailty is an emerging yet controversial concept.[18] It is related to age, disability and comorbidity, yet it is distinct from these concepts.[15] The determinants of frailty are a mix of physiological, psychological, social, and environmental factors. Fried and Walston[19] proposed a frailty phenotype[b] that included three physiological determinants; sarcopenia, neuroendocrine dysregulation, and immunologic dysfunction, all of which interact to cause physical frailty[c]. Frailty becomes more prevalent with age.

Forty-six percent of community-dwelling older adults above the age of 85 are considered frail.[19] Although one's risk increases with age, frailty may exist independently of age.[15] For example, an 80-year older adult may be healthy whereas another individual of the same age may be severely frail. Frailty is related to disability, but disability may occur independently of this geriatric syndrome.[20] Only 27% of older adults who are dependent for ADL are considered frail.[13] Comorbidity is also often falsely treated as a synonym of frailty as it may exist independently of this syndrome.

[a] A margin of safety that allows a system to survive during failure
[b] The observable characteristics, at the physical, morphologic, or biochemical level, of an individual, as determined by the genotype and environment
[c] A state of pure physiological vulnerability

Fried et al.[13] reported that 32% of frail older adults did not have any comorbidity. Although frailty is related with disability and comorbidities for both men and women, frailty is more common in women than men.[13]

At any given age women are frailer than men.[21] Age-related decline of muscle mass and strength likely cause women to transition into frailty earlier than men due to their naturally lower physiological reserve capacity.[13] Both men and women have higher mortality rates as level of frailty increases; however, women have lower mortality rates compared with men of the same frailty level.[22] The relationship of frailty with age and sex is comparable across countries;[22,23] yet, there are differences in the prevalence of frailty between countries and races.[24,25]

The majority of frailty studies have been conducted in North America, but recent investigations suggest that frailty may be more prevalent in Europe as a result of social and environmental factors.[20,25,26] Research on frailty is very limited in the developing countries. Gu et al.[23] reported similar results to those already recorded in more developed countries, in that frailty in Chinese older adults is more prevalent with advanced age and is highly associated with mortality. They also reported differences in the prevalence of frailty across various Chinese ethnic groups. Greece is a country of interest for many gerontological researchers because it has one of the oldest populations in Europe (19.2% of the population over the age of 65).[27] Within the Greek older adult population, 45% are at risk for frailty, and 15% are already considered frail.[25] Due to the rapidly aging population across all countries, frailty should be identified early to prevent the human and economic burden associated with this syndrome.

1.2 Tools to Identify Frailty

Frailty is a measurable syndrome both clinically and in the community.[28] Criteria have been proposed to diagnose frailty in relation to the determinants of frailty. However, currently none of the proposed operational definitions of frailty that examine these criteria provide a definitive diagnosis of frailty.[5,13] Most operational definitions include mobility, balance, muscle strength, motor processing, cognition, nutrition, endurance, and physical activity as criteria of frailty.[12,13,17,29-31] The most commonly used operational definitions are the Frailty Phenotype[13] and the Frailty Index (FI).[32] Other frailty assessment tools include; Frailty and Vigorousness Classification,[33] Study of Osteoporotic Fractures frailty measure,[34] and the Edmonton Frail Scale.[35]

Fried et al.[13] demonstrated that five physical criteria (muscle weakness, subjective fatigue, reduced physical activity, low gait speed, and weight loss) could be used to determine a physical frailty phenotype. Three or more of these criteria indicate frailty, one to two criteria indicate a pre-frail condition, and no indicators suggest the individual is not frail. This three-level classification has strong content, construct, concurrent, and predictive validity.[13,36] Identification of physical frailty predicts falls, poor mobility, ADL disability, hospitalization, and death.[13] In addition, it is applicable across diverse population samples.[36]

Ensrud et al.[34] proposed another operational definition of frailty that might be more suitable in a busy clinical practice setting. The three criteria were weight loss, inability to rise from a chair five times without using arms, and reduced energy level. Presence of all these criteria would identify an individual as "frail", one or two would identify him or her as "intermediate frail" and absence of these criteria would identify someone as "non-frail". Similar to Fried's definition,[13] this operational definition was associated to the increased risk of adverse outcomes as the severity of frailty became more apparent. However, its validity is limited solely to older women.

The FI[32] is based on a mathematical model of the accumulation of deficits (e.g. how many things people have wrong with them) where a deficit can be any symptom, sign, disease, disability, or laboratory abnormality. All deficits represent conditions that accumulate with age and are associated with adverse outcomes.[37] The number of deficits present within a person are divided by the total deficits. For example, if the total variables were 60 and 10 deficits were present, then the FI score would be 10/60 = 0.17. The FI does not give a cut point up to which someone is frail, rather it is graded so that the greater the score (closest to one) the more likely that someone is vulnerable to adverse outcomes. People accumulate on average 0.03 deficits per year after the age of 70 with a maximal limit approximately at 0.7.[32,38] The FI predicts worsening health status, institutionalization, and death, and is validated in both community and institutionalized older adults.[38] Prior studies have shown that the FI, even when different deficits are collected, has remarkably similar measurement properties and substantive results especially when a minimum of 30 variables are included.[38] This tool is reasonably easy to use and requires no special instrumentation. However, it may better serve clinicians who have experience in the care of older adults, as it requires experienced clinical judgment.

Speechley and Tinetti,[33] in an effort to identify different types of falls and fallers and better target fall prevention programs, developed a method for screening frailty which classified older adults into vigorous, transitional, and frail categories. The ten criteria that defined these levels were: age, gait/balance, walking for exercise, other types of exercise, depression, use of sedatives, near vision status, upper and lower extremity strength, and lower extremity disability. These criteria were measured through functional tests, physical examination, and health and behavioral questionnaires. Speechley and Tinetti's[33] classification system is shown to be predictive for falls and fall related injuries and was validated in community-dwelling older adults.

The Edmonton Frail Scale[35] proposes ten criteria of frailty; cognition, self-rated health status, hospitalization, functional independence, social support, medication use, nutrition, mood, continence, and mobility. These criteria were either continuous, ordinal, or binary variables. The binary variables were re-coded using the convention that "0" indicates the absence of a deficit and "1" the presence. The ordinal and continuous variables were re-coded between "0" and "2" based on the levels of the variable. The maximum score is 17 and the higher the score the greater the severity of frailty. This scale has good construct validity, reliability, and internal consistency, is brief and does not require clinical judgment.[35]

There is currently no gold standard against which frailty scales may be judged. It is likely that some frailty scales might be more successful than others.[39] Van Iersel and Olde Rikkert[40] used four different operational definitions (frailty phenotype, FI, low handgrip strength, and low gait speed) to measure frailty, which resulted in highly different selections of older adults for each definition. Herrmann et al.[9] examined how nurses, medical residents and chief medical residents perceive frailty and concluded that these health care professionals characterize different kinds of people as frail because they do not have the same perception of frailty. Before researchers and health professionals decide upon use of a frailty assessment tool they should examine which measure is the most appropriate based-upon the purpose, the similarities between the population under investigation and the validation group, and the quality of the validation process.[40] For example, researchers who focused solely on physical frailty may find Fried's operational definition more predictable whereas practitioners who are interested in other components of frailty might find the FI, the Edmonton Frail Scale or the Frailty and Vigorousness Classification to be more meaningful. For the purpose of this thesis the Frailty Phenotype[13] and the FI[32] were used to assess frailty in the included studies. Regardless of the operational definition used to assess frailty, some measure of physical function should be included as a criterion of this geriatric syndrome.[12]

1.3 Frailty and Physical Function During Performance-Based Tasks

Performance-based measures of physical function are essential criteria for frailty.[12,41] Poor performance on tests of physical function (e.g. muscle strength and walking) predicts falls, disability, hospitalization, and death in older adults.[42-46] These tests may offer a clearer understanding about relevant assessment, treatment and rehabilitation pathways than traditional clinical and self-reported measures.[47,48] Laboratory and functional performance measures are important, but limited for this population. Most laboratory tests developed for older adults are not applicable to those who are frail. In addition, frail older adults are often unable to attend a laboratory for testing due to their impaired health. Thus, the development of standardized measures of physical function that may be reliably performed by frail older adults within their home environment are highly desirable.[12] Recent research suggests that impaired muscle function and ambulatory mobility are primary criteria of frailty and may be used to measure changes in frailty status;[12,30] yet, assessment protocols for these criteria often differ across studies.[49]

Impaired muscle function is one of the main contributors of frailty and has been examined more than other risk factors (neuroendocrine dysregulation and immunologic dysfunction).[13] Frail older adults have reduced muscle mass and strength and greater fat mass than non-frail older adults.[26] Therefore, frail older adults probably need to engage relatively more of their maximal strength to simply perform ADL as compared to non-frail or younger adults.

Fried et al.[13] utilized low isometric handgrip strength as a criterion of frailty as have others.[24,36,50-57] Although isometric handgrip strength is thought to be a good predictor of adverse health events[46] it is limited to only the upper limb, usually the dominant hand, and may not entirely capture the role of lower extremity weakness causing frailty.[26] Studenski et al.[30] reported that handgrip, upper and lower body strength were indicators of changes in frailty status. Speechley and Tinetti[33] stated that changes in frailty status could be predicted by reduced strength around the knee and shoulder joint. Others have suggested using chair stands as a criterion of frailty.[34,58-60] Muscle function has been extensively used as a criterion of frailty and there is an urgent need for agreement on the assessment protocol of this concept when used to predict frailty. It is reasonable to suggest a measure of lower body strength given its importance for remaining mobile.

Impaired motor control and slowed gait speed are readily observed in frail older adults.[12] Ambulatory mobility, another measure of physical function, was tested in many studies as a criterion of frailty using various protocols; 50-foot (~ 15 meters) walk test,[58] 15-foot (~ 4.5 meters) walk test at preferred pace,[13,24] 4-meter walk test at preferred pace,[36,50-54] 8-foot (~ 2.5 meters) walk test at preferred pace,[55,60] and 10-foot (~ 3 meters) up-and-go test at maximal pace.[35,56,57,59] The measures of ambulatory mobility are considered to be essential criteria of frailty. However, those measures that capture the daily life of older adults may provide a greater understanding about frailty.

1.4 Frailty and Daily Life Measurements

Daily activities are often reported to be "hard work" for most frail adults.[61] Frail adults live close to thresholds of physical ability where an acute adverse event precipitates the older adult into a state of frailty.[12] Decline in physiological reserve capacity will make ADL seem difficult to complete often leading to physical inactivity. However, we don't know if these changes leading to physical inactivity are preceded by changes in muscle activity or vice versa. Measuring physical and muscle activity together during normal daily life may elucidate our understanding of progressive physiological decline.

Low level of physical activity (PA) is one of the key criteria of frailty[57] and increased PA could prevent or reverse frailty.[62] There are a range of objective and subjective tools designed to measure duration and intensity of PA. These methods are validated for older adults but not for frail older adults.[63-68] Self-report PA questionnaires are the most common method to evaluate PA but are limited due to memory/cognition and recall problems associated with frail older adults.[69] Objective measures of PA include; pedometers, accelerometers, heart rate (HR) monitors and global positioning systems (GPS).[64,67,68,70] Each of these methods has strengths and weaknesses for the evaluation of PA. However, when used in combination, they provide a more comprehensive evaluation of PA during daily life, especially in slow moving frail older adults. To our knowledge no studies have yet used multiple tools to quantify PA in older women across levels of frailty. These measures of PA cannot provide direct information on the intensity of muscle activity performed during ADL, but portable electromyography (EMG) may be an option.

Recent studies have suggested that recordings of daily muscle activity using portable EMG alone or in combination with accelerometers can be used to examine muscle activity in healthy community-living middle-aged and older adults.[71-73] Portable EMG may provide information on the intensity of daily PA, paralleling the information provided when EMG is used to assess workplace demands.[74-78] Daily upper and lower limb muscle activity and quiescence is a result of an interaction of several systems (e.g. muscular and nervous system) and may be a more complete indicator of health status and a more precise indicator of frailty. Recent studies measuring muscle activity during daily life and discrete tasks reported muscle activity was greater in non-frail older adults relative to young adults. In addition, this age-related difference was greater in women compared with men.[71,79] Muscle activity and quiescence recorded during daily life in older women across various levels of frailty is yet unknown, but could contribute to our understanding of the progression of this syndrome and the dissociation of its levels.

1.5 Levels of Frailty

The development of the frailty syndrome is a slow and insidious process, individually specific and unique in its presentation. The eventual diagnosis is often made too late along the clinical pathway making treatment complex and challenging.[28] There is a paucity of evidence regarding the capacity of health care professionals and the general public to recognize and manage frailty in community settings before it contributes to significant functional dependency. Even though the majority of frail older adults live in the community, most of the studies on frailty have been done in hospitalized or nursing home populations.[16] In addition, most people who arrive in these settings usually have the highest levels of frailty and may have already experienced significant adverse outcomes (i.e. fall and/or fracture).[13]

Measuring levels of frailty has proven to be more challenging. Rockwood et al.[29] argue that a successful operational definition of frailty should identify clinically recognizable levels of frailty. Frailty ranges in form from mild to severe,[12] and it is possible that lower levels of frailty (less severe) might be associated with different factors than higher levels of frailty (more severe).[13] For example, at lower levels of frailty weight loss may be the result of malnutrition, whereas reductions in body mass and accompanying muscle weakness that occur during higher levels of frailty may involve more complex interactions across multiple factors such as; malnutrition, catabolism, injury, and inflammatory disease.[19] Lower levels of frailty are most often observed in community-dwelling older adults, whereas higher levels of frailty are more common in nursing home populations.[13,56] One recent study found that over half of community-dwelling older adults were considered at risk, thus living perilously close to becoming frail while 7% were already frail.[56] Frailty is a dynamic process, but the transition to higher levels of frailty is more common than the transition to states of lesser frailty. However, transitions to less frail clinical states and even from being frail to nonfrail is a possibility.[56]

1.6 Management of Frailty

Frailty confers an array of adverse outcomes most often identified during an acute or sub-acute presentation. The current research literature has shown that such presentations are potentially amenable to prevention, early identification, assessment and rehabilitation.[12,56,58] Although we have no way to impact the underlying biological process, frailty criteria are modifiable and therefore can be prevented and treated.[12,56,58] Hence, it is of value to delay or prevent the onset of frailty.[80] Different interventions may be appropriate based-on the level of frailty.[81] In addition, the level of frailty, age and physical function play a role in the effectiveness of the intervention.[18]

Lower levels of frailty may be assumed to be the most responsive to intervention[82] through management of underlying morbidity and deconditioning. Targeting those in this level may make a significant difference in reducing frailty among community-dwelling older adults. If frailty is detected early (those at risk for frailty) then interventions can be used to restore and/or maintain functional independence, prevent further progression toward frailty,[12] and even facilitate transition back to a non-frail level.[56]

Although there may be debate on how to clinically measure the concept and levels of frailty, especially in circumstances where time is of the essence,[34] there is little doubt about its impact on the older individual, the family and society as a whole. At both the population and social level, mounting evidence suggests that public education, preventative interventions and adhering to a healthy lifestyle, early in the aging process, may reduce the incidence of frailty.[83]

Community health care professionals will become increasingly exposed to frail older adults and therefore require a better understanding of frailty, including the interventions that can improve the clinical outcomes of frailty. An integrated health care system with an effective collaboration between health care professionals is essential to delay or prevent the onset of this syndrome in older adults.[80] Emphasis should be on those health professionals (e.g. family physicians, nurse practitioners, physiotherapists, occupational therapists and nurses) who regularly treat older, reasonably independent, community-dwelling adults and can most often identify low levels of frailty before it is too late. By identifying individuals "at risk" and intervening early on, by preventing or mitigating the impact of disease and increasing fitness, it may be possible to compensate for the underlying biologic process of senescence.

Mounting evidence suggests that exercise interventions can be used to restore and/or maintain functional independence in older adults[84,85] and may potentially prevent, delay or reverse the frailty process.[56] The American College of Sports Medicine's (ACSM) position stand[86] on exercise for older adults recommends that exercise prescription for frail people is more beneficial than any other intervention and that the contradictions to exercise for this population are the same as those used with younger and healthier people. In addition, the most recent updated ACSM guidelines[87] recommend that resistance and/or balance training should precede the aerobic training for this population. However, recommendations on the appropriate design of the exercise protocol were not included. An updated systematic review of exercise interventions for frail older people, that comprehensively examines how frailty is assessed and does not focus only on one specific outcome measure, has yet to be completed.

1.7 Thesis Outline

The aims of this thesis were: 1) Examine performance-based physical function and daily muscle and PA in older women across levels of frailty; and 2) Review the effectiveness of current exercise interventions for the management of frailty. The first chapter (Chapter 1) provided background information about the topic of this thesis and the rationale for why we conducted the four studies. The thesis consisted of four studies. The first three studies (Chapters 2, 3 and 4) reported data from an observational study of community-dwelling older women from rural Greece. The fourth study (Chapter 5) presents the results of a systematic review. The aim of the first study (Chapter 2) was to determine which performance-based measures of physical function are most closely related to frailty and whether physical function is different across levels of frailty. The second study (Chapter 3) examined the association of frailty with daily PA measured with multiple objective and self-reported methods. The aim of the third study (Chapter 4) was to determine whether daily muscle activity in upper and lower limb muscles differs in older women across levels of frailty. The fourth study (Chapter 5) systematically examined the literature about the use of the term "frailty" in relation to exercise interventions and their effectiveness on preventing and/or reversing frailty. The final chapter (Chapter 6) summarized the findings of the thesis and provides recommendations for future research. The overall aim of these research investigations was to provide a more focused understanding about the physical function of older women across levels of frailty during performance-based tasks and daily life and to emphasize the importance of including frail older adults in future gerontological research.

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CHAPTER 2

Relationship Between Frailty and Physical Function Performance-Based Measures[a]

2.1 Introduction

Frailty is an age-related state of vulnerability to adverse outcomes, which has a devastating impact on older adults, their family, and society. Frailty is more common in older women than men.[1] Although frailty has a complex etiology it is measurable both clinically and in the community.[2] Many operational definitions of frailty now compete,[3] of which the most commonly used are the Frailty Phenotype,[4] and the Frailty Index.[5] Although these operational definitions identify groups of people at high risk, they do not necessarily recognize the same individuals as being frail older adults.[6-9] Criteria proposed as clinical markers of frailty include ambulatory mobility, muscle strength, balance, motor processing, cognition, nutrition, endurance and physical activity.[3,4,10-14]

Performance-based physical function measures have been proposed as essential criteria for frailty.[10,15] Poor performance on tests of physical function (e.g. muscle strength and walking) predicts falls, disability, hospitalization, and death in older adults.[16-20] These tests are said to offer a clearer understanding about relevant assessment, treatment and rehabilitation pathways than traditional clinical and self-reported measures;[21,22] however, there is presently no agreement on the specific tools needed to measure these criteria. Multiple researchers have suggested that impaired muscle function and ambulatory mobility are primary criteria of frailty and may be used to measure changes in the frailty status;[10,13] however, assessment protocols differ across studies. Recruiting frail people for studies that require them to visit a laboratory may be

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challenging and preclude frail older adults from participation.[23] Thus, the development of standardized measures of physical function that may be reliably performed by frail older adults within their home environment is highly desirable.[10] The specific objectives of this study were: 1) Examine which performance measures of physical function are most closely related to frailty; and 2) Determine if physical function is different across levels of frailty.

2.2 Methods

Fifty-three community-dwelling women aged 63-100 years who were living in rural areas within the prefecture of Thessaloniki, Greece participated in this study. Research approval for this investigation was granted by the Human Ethics Research Board and informed consent was received prior to participation.

The researcher visited participants' homes on three occasions. The first visit entailed administration of a health history questionnaire, which was used to determine the level of frailty using the Frailty Index.[5] Measurements of agility and dynamic balance, handgrip muscle strength and fatigue, walking performance, and lower body isotonic muscle strength were also assessed. To minimize participant burden the researcher returned to the participant's home the subsequent morning to administer the upper body muscular endurance and lower body isometric muscle strength and fatigue tests. At the end of the day, the researcher made a third visit to assess lower body muscular endurance. All measures were carried out by the same investigator (OT).

2.2.1 Frailty Index

A Frailty Index (FI) was constructed based on a mathematical model of the accumulation of deficits where a deficit can be any symptom, sign, disease, disability, or laboratory abnormality that accumulate with age and are associated with adverse events.[5] Care was taken that non performance-based measures were used for the development of the FI for this study, derived from 56 measures within 13 domains that comprise a standard health history questionnaire (adapted from Rogers, 2005[24]) (see Appendix C, Table C.1 for domains, measures and scores for the FI). There were either continuous, ordinal, or binary variables and the number of recorded deficits was then divided by the total measures (56 measures) to give a FI. For example, if 10 deficits were present the FI score would be 10/56 = 0.18. The FI does not give a cut-off which identifies someone as frail, rather it is graded so that the greater the score (closest to one) the more likely that someone is vulnerable to adverse events associated with frailty.

2.2.2 **Muscle Strength**

Maximal isometric and isotonic knee extension (KE) strength of the dominant (self-reported) leg was measured in a sitting position using a portable custom-built chair. Participants sat on the chair (seat height 63 cm) in a comfortable upright position with feet unsupported and the knee and hip flexed to 90 degrees. Straps were positioned diagonally across the chest to prevent forward flexion and the arms were placed on these position belts.

Maximal isotonic KE strength was measured using the adjustable Recordman™ foot weights to determine the participant’s one repetition maximum (1RM). Initially, participants performed three submaximal KE with a light load [~ 2-3 kg (4.5-6.5 lb)] to warm-up. Participants started with the knee joint at 90 degrees and extended the leg upward to approximately 10 degrees of knee flexion (instructed to not fully extended leg). Participants performed approximately 3-5 single repetition lifts using increasing weight loads [~ 0.25-1 kg (0.5-2 lb)] until their 1RM was achieved. The one RM was defined as the maximal weight that the participants could lift, with control, through the full range (80 degrees) of motion.[25]

Maximal isometric KE strength was measured using the Chatillon™ Digital Force Gauge (Ametek Inc, Digital Measurement Metrology, Inc, Mississauga, Canada) dynamometer. The dynamometer was rigidly stabilized to the back leg of the chair corresponding to the dominant side of the participant and in line with the ankle. The participant's ankle was fastened by a belt to the strain-gauge system allowing no KE beyond 90 degrees. Prior to each test the dynamometer was adjusted according to the participant's leg length. After two or three practice trials the participants were asked to perform three maximal isometric KE. The inter-trial rest interval was one minute. The highest of the three measures was used for this analysis.

Handgrip muscle strength was measured using a Martin™ Vigorimeter (Elmed, Addison, USA). The shoulder of the participant was adducted and neutrally rotated, the elbow was flexed at 90 degrees, and the forearm was in neutral position with the wrist slightly extended (0-30 degrees).[26] After two to three practice trials participants were instructed to squeeze the rubber bulb as hard as possible for three consecutive trials. The inter-trial rest interval was one minute. The highest of the three measures was used for the analysis. Both hands were tested and the sequence of dominant and non-dominant hand measures was randomized.

2.2.3 **Muscle Fatigue**

For the handgrip and isometric KE fatigue tests the position was identical to the set-up for the maximal strength tests. The participants were instructed to perform the same contractions (handgrip or isometric KE) as performed for the strength tests; however, for the fatigue tests they were asked to hold the contraction until the force declined to 50% of their maximal strength which was declared as the time to task cessation (seconds). For the handgrip fatigue test the time (seconds) was recorded for each hand (randomized order) whereas for the KE fatigue test only the dominant side was measured. Participants were given verbal encouragement in an attempt to motivate them to achieve maximal effort and the researcher verified that the starting strength corresponded to their established maximal strength.

2.2.4 **Muscular Endurance**

Lower body muscular endurance was evaluated using the chair stand test. From a sitting position, participants rose to full standing and then returned back to the initial seated position. Participants were encouraged to complete as many chair stands as possible within 30 seconds. The total number of chair stands executed within the 30 seconds was recorded.[27]

Upper body muscular endurance was evaluated using the arm curl test. From a sitting position, the participants curled a 2.27 Kg (5 lb) dumbbell from full extension to full flexion with the dominant arm as many times as possible within 30 seconds. The total number of arm curls executed within the 30 seconds was recorded.[28]

2.2.5 **Agility and Dynamic Balance**

Agility and dynamic balance were evaluated using the 8-foot up-and-go test. From a sitting position, participants got up from a chair, walked as quickly as possible around a small traffic cone that was placed 2.44 meters (8 feet) away from the chair, and then returned to a seated position in the chair. After one practice trial, the participants were asked to perform the two consecutive trials with a minute inter-trial rest interval. The lowest time (seconds) of the two measures was used for analysis.[28]

2.2.6 Walking Performance

Participants performed the 15-foot walk test (4.57 meters) at a preferred and maximum speed in a single test session.[4] An additional 1.52 meters (5 feet) were included at the start and the end of the 15-foot walkway to ensure that participants reached a constant gait velocity and were not slowing down at the end of the walking test. For the preferred walking speed condition participants were instructed to "walk at their normal everyday pace" and for the maximum walking speed condition they were instructed to "walk as quickly but as safely as possible". The researcher walked slightly behind the participant to ensure safety, but being careful not to influence their walking speed. Walking time (seconds) and number of steps taken over the 15-foot distance were recorded. Mean Gait Velocity (GV = distance/time) and Stride Length (SL = distance/(steps/2)) were calculated.

2.2.7 Statistical Analysis

The Statistical Package for the Social Sciences (SPSS, Chicago, IL) for Windows version 17.0 was used for this analysis. Pearson product-moment correlations were computed to examine the association between chronological age and FI. Standard multiple linear regressions were performed between the performance-based measures of physical function (dependent variables) and FI and chronological age (independent variables). Univariate relationships between frailty and physical function and between age and physical function were considered (r). Frailty and age were considered simultaneously in relation to each of the physical function measures (R). The independent adjusted relationship between frailty and age with physical function was analyzed (β and sr^2). Participant scores for the FI were split into tertiles. Frailty Index tertiles included the lowest FI tertile (< 0.19 FI), the intermediate FI tertile (0.19-0.36 FI), and the highest FI tertile (> 0.36 FI) (Table 2.1). One-way analysis of variance (ANOVA) was performed to determine whether performance-based measures of physical function differed between the three FI tertiles. Tukey post-hoc tests were run when there was a significant main effect for frailty. Effect sizes between the FI tertiles were also determined. Missing values were replaced by the predicted scores from regression equations of the other variables. A significance level of $p \leq 0.05$ was set. Data reported within the text and in the tables are reported as values ± standard deviation of the mean, whereas figures are presented as values ± standard error of the mean.

Table 2.1. Descriptive Characteristics

	Lowest FI Tertile (n=17)	Intermediate FI Tertile (n=18)	Highest FI Tertile (n=18)
Frailty Index (FI)			
Median	0.11	0.25	0.46
Range	0.03-0.16	0.19-0.36	0.36-0.61
Age (years)			
M ± *SD*	71 ± 4	76 ± 6	82 ± 7*†
Range	65-79	63-90	69-100
Height (cm)			
M ± *SD*	155 ± 4.7	155 ± 5.6	151 ± 7.0
Range	147-162	146-167	138-164
Weight (kg)			
M ± *SD*	68.5 ± 9.4	76.9 ± 11.5	72.7 ± 16.9
Range	52-88	61-99	52-117
Number of Self-Reported Comorbidities			
M ± *SD*	1.7 ± 1.2	2.7 ± 1.5	3.2 ± 2.0*
Range	0-4	1-6	0-7
Number of Prescription Medication(s)			
M ± *SD*	4.2 ± 2.3	5.2 ± 3.0	5.3 ± 3.3
Range	2-9	0-10	0-12

*Significantly different from the lowest FI tertile
†Significantly different from the intermediate FI tertile
FI, frailty index; **M**, mean; **SD**, standard deviation; **cm**, centimeters; **kg**, kilograms
$p \leq 0.05$

2.3 Results

Fifty-three women participated in this study, but 12 did not complete all measures. All 53 participants completed the walking, handgrip, and arm curl tests. Three women refused to attempt the isotonic KE strength, isometric KE strength and fatigue, and the chair stand tests because they thought that they were too old and weak. One of these women did not attempt the 8-foot up-and-go test for the same reason. Four other women did not complete the chair stand tests and five women did not complete the isotonic KE strength test due to knee, hip and/or back pain. There was no difference between the women with missing values and the rest of the participants for chronological age or physical function measures completed by all women; however, women with missing values were considered more frail (0.36 FI; $p = 0.04$)

2.3.1 **Relation Between Frailty, Age, and Physical Function**

The FI was significantly related to chronological age (Figure 2.1). Pearson's product moment correlations suggest that the FI and all physical function measures were significantly related, except for isometric KE fatigue. Pearson product moment correlations between age and physical function were significantly related across all performance tests except isometric KE fatigue and dominant and non-dominant handgrip fatigue (Table 2.2). The proportion of variation in physical function measures predicted from the combination of the FI and age was statistically significant for all measures of physical function except isometric KE fatigue and non-dominant handgrip fatigue (R). Together, 19-71% of the variability in these physical function measures can be explained by knowing the FI and age (R^2). Although the correlation between age and physical function measures was significant for most measures, age did not contribute significantly to the regression analysis for most of them. Age, added only 4-10% to the prediction of walking performance measures, non-dominant handgrip strength, and agility and balance. In contrast, FI's unique contribution after adjustment for age was significant for most measures (except isometric KE and non-dominant handgrip fatigue) and ranged from 11-30%. The physical function measures that were the most closely related to frailty were walking measures (GV and SL), agility and balance, and lower body muscular endurance (30-second chair stands) (Table 2.2).

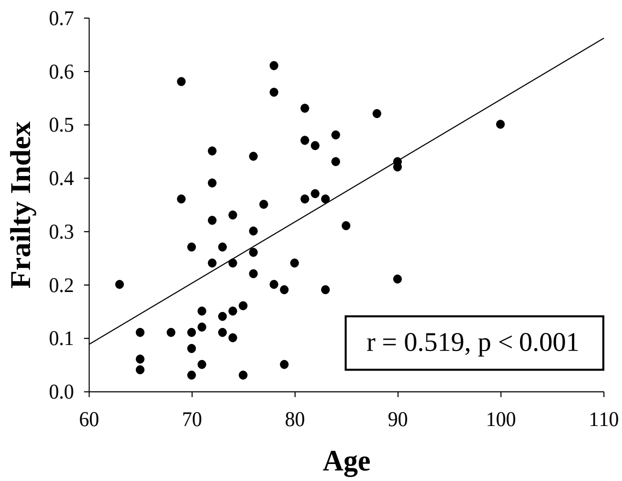

Figure 2.1. The Relationship Between Frailty Index and Chronological Age
r, Pearson correlation coefficient

Table 2.2. Standard Multiple Regression of Frailty Index and Age on Physical Function

Physical Function Variables	r		R	β		sr^2	
	Frailty Index	Age		Frailty Index	Age	Frailty Index	Age
Isotonic KE strength (kg)	-0.64†	-0.50†	0.67†	-0.51†	-0.24	0.19†	0.04
Isometric KE strength (kg)	-0.51†	-0.27*	0.51†	-0.50†	-0.01	0.19†	0.00
Isometric KE fatigue (sec)	0.13	0.01	0.14	0.17	-0.07	0.02	0.00
Dominant handgrip strength (kpa)	-0.52†	-0.47†	0.57†	-0.38†	-0.27	0.11†	0.05
Non-dominant handgrip strength (kpa)	-0.65†	-0.54†	0.69†	-0.50†	-0.28*	0.19†	0.06*
Dominant handgrip fatigue (sec)	-0.44†	-0.21	0.44†	-0.45†	0.03	0.15†	0.00
Non-dominant handgrip fatigue (sec)	-0.29*	-0.21	0.29	-0.24	-0.08	0.04	0.00
Chair Stands	-0.71†	-0.47†	0.72†	-0.64†	-0.14	0.30†	0.01
Arm Curl	-0.58†	-0.47†	0.61†	-0.45†	-0.24	0.15†	0.04
8-foot up-and-go (sec)	0.72†	0.55†	0.75†	0.60†	0.24*	0.26†	0.04*
Mean Gait Velocity-preferred (m/sec)	-0.80†	-0.65†	0.84†	-0.63†	-0.32†	0.29†	0.07†
Mean Gait Velocity-maximum (m/sec)	-0.78†	-0.62†	0.82†	-0.63†	-0.29†	0.29†	0.06†
Stride Length-preferred (m/stride)	-0.77†	-0.61†	0.81†	-0.62†	-0.29†	0.28†	0.06†
Stride Length-maximum (m/stride)	-0.75†	-0.66†	0.81†	-0.56†	-0.37†	0.23†	0.10†

r, Pearson correlation coefficient; **R**, regression correlation coefficient; **β**, Standardized correlation coefficient; **sr**, semipartial correlation; **KE**, knee extension; **kg**, kilograms; **kpa**, kilopascals; **sec**, seconds; **m**, meters

*$p \leq 0.05$, †$p \leq 0.01$

2.3.2 Physical Function Across Tertiles of Frailty

Height, weight, and number of medications were similar among the three FI tertiles. Highest FI women were older than the other two tertiles and had more comorbidities than the lowest FI women. In contrast, no difference was found in number of comorbidities between the lowest and intermediate FI women (Table 2.1). Univariate tests demonstrated a significant main effect of frailty on all physical function measures except isometric KE and non-dominant handgrip fatigue. For these significant main effects, post-hoc testing revealed that the highest FI group scored lower for all physical function measures compared to the lowest FI group (Figure 2.2). Highest FI women had worse physical function than intermediate FI women for isotonic KE strength (Figure 2.2A), non-dominant handgrip strength (Figure 2.2B), upper and lower body muscular endurance (Figure 2.2C), 8-foot up-and-go (Figure 2.2G), GV (Figure 2.2E), and SL (Figure 2.2F) at both paces. No differences were found in the isometric KE strength (Figure 2.2A) and dominant handgrip strength and fatigue (Figure 2.2B and 2.2D) between the highest and intermediate FI tertiles. The intermediate FI tertile was weaker for dominant and non-dominant handgrip strength and had slower walking speed and shorter stride length compared with the lowest FI women. Isotonic and isometric KE strength, dominant and non-dominant handgrip fatigue, arm curl endurance, and 8-foot up-and-go scores were similar between intermediate and lowest FI women.

The effect sizes (ES) calculated from the univariate tests between the frailty tertiles revealed the greatest decline in physical function occurred between the lowest and highest FI groups (ES 1.10-3.33). The decline in physical function between the lowest and intermediate FI groups (ES 0.99-1.60) was less than the decline between the intermediate and highest FI groups (ES 0.94-1.82), except for the handgrip strength tests. The physical function measures that declined the most between the lowest and intermediate FI groups were GV, SL, and chair stand test. The physical function measures that declined most between intermediate and highest FI groups were GV, SL, and 8-foot up-and-go scores. The physical function measures that declined the most between the lowest and highest FI groups were the GV, SL, and chair stand test (Table 2.3).

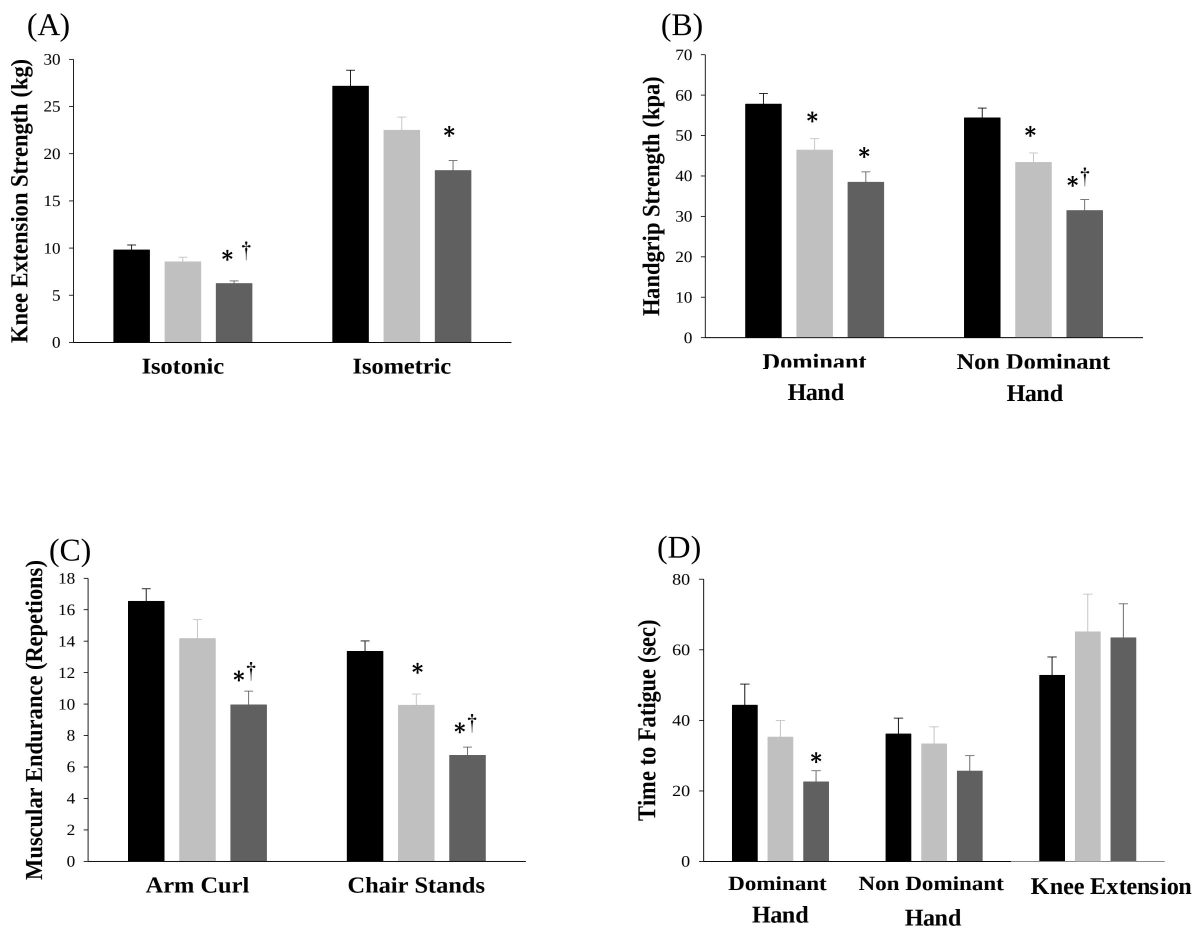

Figure 2.2. Measures of Physical Function Across Frailty Tertiles
(A) Knee extension strength; (B) Handgrip strength; (C) Muscular endurance; (D) Handgrip and knee extension time to fatigue

(Figure 2.2 continued pg.35)

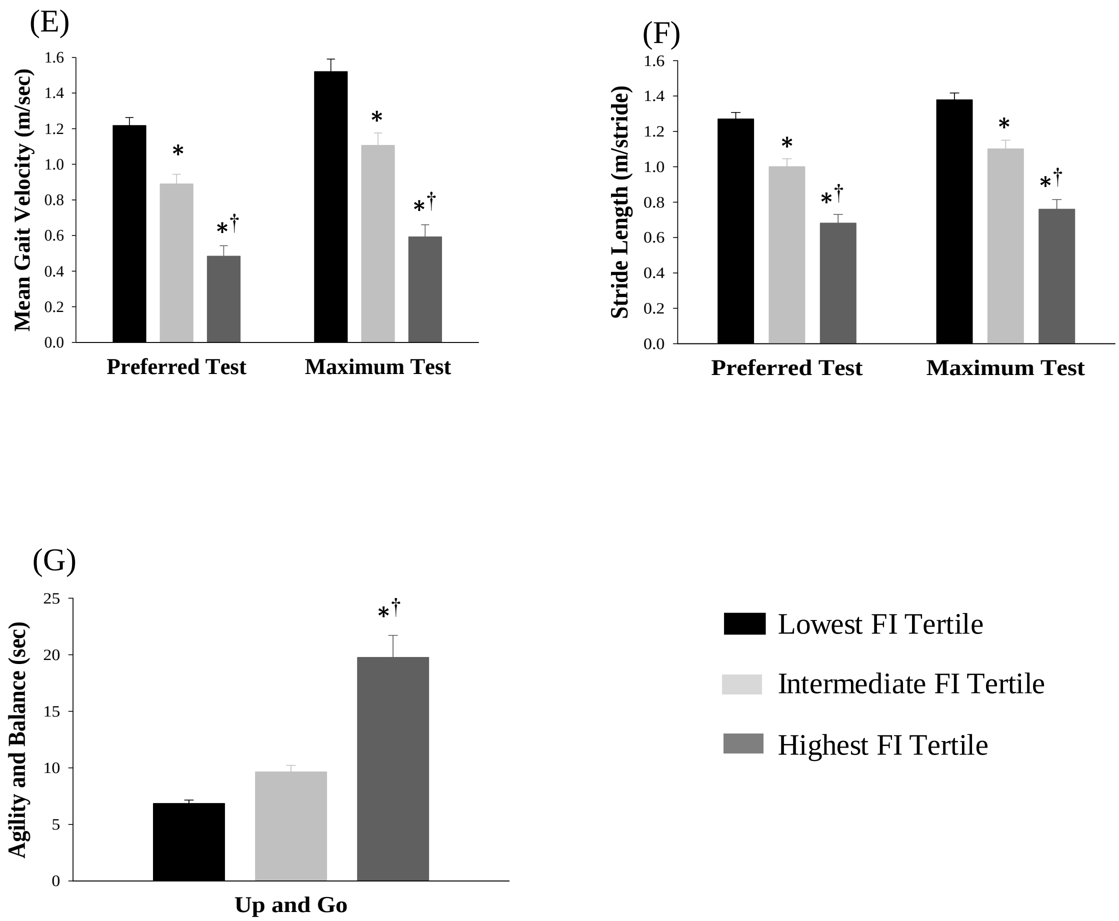

Figure 2.2. (Continued)
(E) Mean gait velocity; (F) Stride length; and (G) Agility and balance
FI, frailty index; **kg**, kilograms; **kpa**, kilopascals; **sec**, seconds; **m**, meters
*Significantly different from the lowest FI tertile; †Significantly different from the intermediate FI tertile
$p \leq 0.05$

Table 2.3. Effect Size of the Relationship Between Frailty and Physical Function

Physical Function Variables	Lowest vs Intermediate FI Tertile	Intermediate vs Highest FI Tertile	Lowest vs Highest FI Tertile
Isotonic KE strength (kg)	NS	1.34	2.04
Isometric KE strength (kg)	NS	NS	1.53
Isometric KE fatigue (sec)	NS	NS	NS
Dominant handgrip strength (kpa)	0.99	NS	1.77
Non-dominant handgrip strength (kpa)	1.15	1.10	2.15
Dominant handgrip fatigue (sec)	NS	NS	1.10
Non-dominant handgrip fatigue (sec)	NS	NS	NS
Chair Stands	1.18	1.19	2.64
Arm Curl	NS	0.94	1.86
8-foot up-and-go (sec)	NS	-1.66	-2.15
Mean Gait Velocity-preferred (m/sec)	1.60	1.75	3.33
Mean Gait Velocity-maximum (m/sec)	1.43	1.82	3.21
Stride Length-preferred (m/stride)	1.56	1.59	3.22
Stride Length-maximum (m/stride)	1.50	1.55	3.11

FI, frailty index; **KE**, knee extension; **kg**, kilograms; **kpa**, kilopascals; **sec**, seconds; **m**, meters; **NS**, not significant

2.4 Discussion

The association of frailty with performance-based physical function was examined in 53 older women from rural Greece. Frailty, measured using a FI, was a better predictor of physical function than chronological age. The best measures of physical function associated with frailty were walking performance (GV, SL) and lower body muscular endurance. Walking at a preferred pace was more related to frailty than walking at maximal pace. In addition, grip strength of the non-dominant hand had stronger correlation with frailty compared to the dominant hand. Physical function differed between levels of frailty and the decline in physical function accelerated after the intermediate FI tertile.

The sample size of this study is small, thus data must be interpreted with caution. Even so, it was large enough to demonstrate the nature of the relationship between age and frailty; frailty is clearly age associated, but is not the same as chronological age.[1,29] For example, within this study a 63- and a 90- year old woman each had the same FI score (0.2), and frailty was only moderately correlated with chronological age. The FI characteristics (median FI score 0.2; maximal FI score 0.6) reported from our small sample is similar to those reported in the larger cohort studies (e.g. Canadian Study of Health and Aging, Australian Longitudinal Study on Aging) which suggests our sample to be representative of the larger population.[9,30-32] Both frailty and chronological age were correlated with physical function but frailty had the stronger relationship. This is not surprising since frailty was noted to be a better measure of health-status and predictor of mortality than chronological age in samples of community-dwelling and institutionalized people.[30] After an adjustment for age, frailty remained correlated with physical function, thus the association of frailty with physical function cannot be explained solely by the influence of age.

Most physical function measures tested were performed by all community-dwelling older adults in our study, except the lower body muscle function tests and the 8-foot up-and-go test. The physical function measures that best predicted frailty were ambulatory mobility (walking and 8-foot up-and-go) and lower body muscular endurance (30-second chair stands). There is strong evidence that lack of ambulatory mobility is associated with adverse health outcomes and it has recently been proposed as the best single indicator of frailty.[33,34] Ambulatory mobility is a complex task and will be affected by frailty more than other less complex tasks (e.g. muscle strength). In addition, walking performance at preferred and maximal pace is strongly correlated with frailty. However, similar to our study Brown et al.[15] reported that walking at a preferred pace had a slightly stronger association with frailty than did walking at a faster pace. This may be related to frail older adults choosing a more stable walking pattern during their normal walking pace, perhaps as a protective measure to avoid falls.[35] Evaluating walking speed and stride length across timing constraints likely yields information about adaptive gait strategies to conditions encountered during daily life relative to environmental conditions and constraints (e.g. pedestrian cross walk time; the frailest group had an average maximal walking velocity of considerably less than 1 m/sec).

Lower and upper body muscular endurance were better predictors of frailty than muscle strength. Muscular endurance is likely a stronger functional measure than strength because activities of daily living (ADL) typically do not require maximal effort but rather sustained submaximal effort.[17,18] Furthermore, isotonic muscle strength was a better predictor of frailty than isometric strength, the former measure being more relevant to physical performance during ADL.[36-38] Handgrip muscle fatigue was correlated with frailty whereas KE muscle fatigue was not. The effect of age on muscle fatigue is equivocal due to various contraction types, protocol durations, and muscles studied.[39,40] Moreover, frailty and muscle fatigue are closely related due to common biomedical determinants[41] and extensive investigation is necessary to understand the role of fatigue relative to frailty rather than mere chronological age.

Dominant handgrip strength is frequently used as an indicator of frailty.[4,42,34] In this study dominant handgrip strength was related to frailty but this relationship was not as strong as shown by the effect sizes as isotonic dominant leg strength, lower body muscular endurance, and upper body muscular endurance. Brown and colleagues[15] also reported that lower body strength tests had stronger correlations with frailty than handgrip strength tests. In addition, poor KE strength is related to subjective fatigue, a common frailty indicator, more than handgrip strength.[43] Non-dominant handgrip strength was more correlated with physical function than the dominant hand. Previous studies[44,45] reported that non-dominant handgrip strength is more related to physical function and osteoporotic fractures than the dominant hand. Possible reasons may be that healthy older adults equally use both hands[46] but frail older adults may use only their dominant hand for ADL. Bonilhia et al.[47] reported that age-related changes in the dominant hand region of the brain were greater than the non-dominant hand region, and another investigation indicated that osteoarthritis was more prevalent in the non-dominant hand than the dominant hand.[48] Ultimately, more studies are needed to examine the role of dominance, especially whether differences exist between lower limbs. The main reason that handgrip strength is used so extensively is that it is inexpensive and easy to administer. However, the lesser used chair stand test and arm curl test are also easy to administer and quite economical.

The physical function measures that discriminated early and later stages of frailty were walking speed, stride length, lower body muscular endurance, and non-dominant handgrip strength. The decline of walking speed was steeper at the later stages of frailty whereas the decline in stride length, lower body muscular endurance and non-dominant handgrip strength was similar at the early and later stages of frailty. Dominant handgrip strength discriminated only early stages of frailty whereas isotonic KE strength, upper body muscular endurance, and agility discriminated only later stages of frailty. Frailty ranges from mild to severe,[3,10] and it is possible that early stages of frailty might be associated with other factors than later stages of frailty.[4] This was supported by the findings of our studies where early stages of frailty were more associated with changes in speed and stride length during walking and lower body muscular endurance whereas later stages of frailty was more associated with walking speed, agility, and isotonic KE strength. Although the sample size was small and many measures were assessed, the association between frailty and most of these measures was significant. The power for the non-significant associations was low, thus establishing a clinical association between these measures and frailty is premature, but a hierarchy of associations of frailty with all measures was evident.

Analyses from physical function measures highlighted that the criteria selected to define frailty and the measurement protocols for these criteria are important; thus comparison between various published studies in the literature needs to be made with caution.[7-9] However, this issue is minimized for the FI because prior studies have shown that with different criteria tested across different populations the FI has remarkably similar measurement properties and substantive results.[7,49] For the purpose of this study the FI was constructed without using performance-based measures of physical function, although these measures are also quite valuable, and should be utilized to define frailty especially for studying frailty at an individual level. Frail older adults experience impairments in many domains of physical function, thus definitions of frailty need to combine various physical function performance-based measures targeted for the management of frailty.[10]

This study examined numerous performance-based measures of physical function believed to be associated with frailty. The useful predictors identified were ambulatory mobility, lower body muscular endurance, and non-dominant handgrip strength. These measures should be included as identifiers within frailty where future investigations will help classify their potential role in preventing further functional decline as well as human and economic burden associated with this syndrome.

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CHAPTER 3

A Comparison of Physical Activity Tools in Older Women Across Levels of Frailty

3.1 Introduction

Epidemiological studies demonstrate a strong relationship between low levels of physical activity (PA) and functional decline, comorbidity, and mortality in healthy older adults.[1,2] Although a large proportion of older adults consider themselves to be healthy a significant proportion may be considered frail.[3] Frailty is an age-related state of vulnerability to adverse outcomes, caused by cumulative declines across multiple physiological systems and ranges from mild to severe.[3,4] Greece is an interesting country for gerontological research because it has one of the oldest populations in Europe (19.2% of the population is over the age of 65).[5] Within the Greek older adult population 45% are at risk for frailty and 15% are already considered frail.[6] Low levels of PA is one of the key indicators of frailty[7] and increased PA could prevent or reverse frailty.[8]

Levels of PA are different between older men and women.[9] Non-frail Greek older women accumulate more daily PA than older men; however, Greek older men perform more bouts of moderate intensity activity throughout the day.[10] Regardless of sex differences, PA levels are generally lower in Greek older adults compared with other European countries.[11] The current recommendation for PA to improve health in older adults is a minimum of 30 minutes, progressing to 60 minutes, of moderate intensity activity on most days of the week.[12] However, most older adults do not achieve this goal.[9] A range of objective and subjective tools has been proposed to measure duration and intensity of PA. These methods have been validated for older adults but not for frail older adults.[13-18] Self-report questionnaires are the most common method to evaluate PA but are limited due to memory/cognition problems of frail adults and their inability to recall what tasks they did during the day.[19] Objective measures of PA include; pedometers, accelerometers, heart rate (HR) monitors and global positioning systems (GPS).[14,17,18,20] In addition, recent studies have suggested that recordings of daily muscle activity using portable electromyography (EMG), either singularly or in combination with accelerometers enable consideration of underlying muscle activity in middle-aged and older adults[21-23] and might provide information on intensity of daily activity, paralleling the information provided when EMG is used to assess workplace demands.[24] Each of these methods has strengths and limitations for the evaluation of PA, but the unique measures each affords, when used in combination, might permit a more comprehensive evaluation during daily life, especially in slow moving frail older adults.

The purpose of this study was to examine the association of frailty with five different PA measurement tools: 1. Accelerometer; 2. HR monitor; 3. Portable EMG; 4. GPS, and 5. Short version of the Minnesota Leisure Time Activity Questionnaire (MLTAQ). The specific objectives were: 1) Examine convergent validity between the total duration and intensity of PA as determined by five PA measurement tools in older adults across levels of frailty; 2) Examine which PA measures are most closely related to frailty; and 3) Determine which PA measures best describe differences in physical function across levels of frailty.

3.2 Methods

A convenience sample of 50 community-dwelling women aged 63-90 years who were living in rural areas within the prefecture of Thessaloniki, Greece participated in this study. The study was approved by the University of Western Ontario Institutional

Human Ethics Research Board and informed consent was received prior to participation. The researcher visited each participant's home on three separate occasions during weekdays. The first visit entailed determining the participant's level of frailty using the Frailty Index[25] by administering a health history questionnaire and physical function performance tests (handgrip muscle strength, upper and lower body muscular endurance, walking speed, agility and dynamic balance). In addition, a PA questionnaire was administered. The researcher returned to the participant's home the subsequent morning approximately one hour after the participant awoke. An accelerometer, HR monitor, EMG device, and GPS watch were attached to the participant. Maximal Voluntary Exertions (MVE) for the vastus lateralis and biceps brachii were performed. Participants were then instructed to proceed with their normal daily activities while wearing the devices and were encouraged to ignore the equipment and undertake a typical day. Bathing was not permitted to prevent damage to the recording devices. Approximately 10 hours later the researcher returned to the home to remove the equipment.

3.2.1 Frailty Index

A Frailty Index (FI) was constructed based on the accumulation of deficits where a deficit can be any symptom, disease, or disability that accumulates with age and is associated with adverse outcomes.[25] The FI for this study was derived from 59 measures identified from a health history questionnaire and/or five physical function performance tests (handgrip muscle strength, upper and lower body muscular endurance, walking speed, agility and dynamic balance) (see Appendix C, Table C.2 for domains, measures and scores for the FI). There were either continuous, ordinal, or binary variables and the number of recorded deficits was then divided by the total measures to give a FI. For example, if 10 deficits were present the FI score would be 10/59 = 0.17. The greater the score (closest to one) indicates increased vulnerability to adverse outcomes associated with frailty.

3.2.2 **Accelerometer**

Participants wore an ActiTrainer (8.6 x 3.3 x 1.5 cm; 51 g; Actigraph, LLC, Fort Walton Beach, FL) for the 10-hour testing. The ActiTrainer has a uniaxial accelerometer (GT1M ActiGraph) programmed to record data in 1-min epochs. The ActiTrainer was secured in a holster, attached to a belt worn at the waist on the dominant side parallel to the mid-axillary line. Physical activity movement data were downloaded into the ActiLife software (Actigraph, LLC, Fort Walton Beach, FL) and acceleration- and step-counts per minute were used to calculate the total number of steps, number of acceleration counts, time spent in activity (cut-off value > 50 acceleration counts/minute), time spent in moderate/vigorous activity (cut-off value > 1041 acceleration counts/minute), and acceleration counts per minute during active time.[13]

3.2.3 **Heart Rate Monitor**

A Polar WearLink 31 coded transmitter (Polar Electro, Kempele, Finland) was worn on the chest with an elastic belt. HR data were wirelessly transmitted to the ActiTrainer and stored as average beats per minute over 1-minute epochs. ActiLife software was used to download and time-match the HR values with the accelerometer data. Recorded HR values were transformed into percentage of HR reserve utilizing the formula %HRR = [(HRactivity - HRrest)/ (est. HRmax – HR rest)]*100. HRmax was estimated using the formula HRmax = (208 – 0.7 * age).[26] Time spent in activity (cut-off value > 20% HRR) and time spent in moderate/vigorous activity (cut-off value > 40% HRR) were calculated.[27]

3.2.4 **Electromyography**

Muscle activity was measured with a portable surface EMG device (Biometrics DataLOG P3X8, Gwent, UK). Surface electrodes were placed mid-belly on the biceps brachii (BB) and vastus lateralis (VL) on the self-reported dominant side and a common ground electrode was worn on the lateral malleolus of the fibula. The inter-electrode distance was fixed at 20 mm and the EMG data logger (9.5 x 15.8 x 3.3 cm; 380 g) was secured to a belt worn at the waist. The signals from the electrodes was sampled at 1,000 Hz, amplified (1,000x), band-pass filtered (20-450 Hz), and stored on a 512 MB MMC flashcard. Isometric maximal voluntary exertions (MVE) were performed for the two muscles (VL, BB) in order to normalize the long-term EMG recordings to a percentage of the participant's maximum. The MVE was executed against experimenter resistance and recorded in the seated position with the joint of interest at ~ 90° for isometric knee extension and elbow flexion. Each muscle was tested in a randomized order three times with 60 seconds rest between trials. The greatest of the three trials was used for normalization of the long-term EMG data. Verbal encouragement was provided by the researcher to ensure maximal effort.

All EMG data during the MVE and the 9-hour testing were imported into Biometrics software (Biometrics DataLog version 3, Gwent, UK) for preliminary visual inspection and subsequently into Spike 2 Version 5 (Cambridge Electronics Design, Cambridge, UK) for analysis in custom software. Data artefacts (~ 5% of the total time) were manually removed across both channels in a time-locked fashion. Signals were rectified, smoothed (time constant 0.01 seconds) and down-sampled (factor of 100). Bursts, defined as a period of EMG activity greater than 2% of MVE for durations longer than 0.1 second, were computed to quantify muscle activity throughout the 10-hour testing period. Number of bursts and total recording time occupied by bursts were calculated. Previous research has used burst analysis to quantify muscle activity in older adults.[21]

3.2.5 Global Positioning System

Participants wore the Garmin Forerunner 405 GPS watch (4.8 x 7.1 x 1.6 cm; 60 g; Garmin International Inc., Olathe, KS) during the 10-hour testing session. GPS data were uploaded to the Garmin training center software (Garmin International Inc., Olathe, KS) and saved in formats appropriate for Google Earth (Google, Inc., Mountain View, CA) and Microsoft Excel (Microsoft Corp., Redmond, WA). Google Earth was used to create maps to define activity that took place at home or away from home. After the start and end points of outdoor activities were identified from Google Earth, GPS data were downloaded into Microsoft Excel for analysis. When the participants were indoors the satellite signal was frequently lost; therefore, only GPS data recorded outdoors were included in the analysis. Distance and time travelled in a vehicle (speed > 3 m/sec for > 1 min), as well as walking time, distance, and speed were calculated. GPS data during walking outdoors were manually time-matched with the accelerometer data and the mean acceleration counts per minute during walking outdoors was calculated.

3.2.6 Self-Report PA

The Short version of the Minnesota Leisure Time Activity Questionnaire (MLTAQ) was administered to the participants.[28] Participants were asked about the frequency and duration of time spent in 18 activities during the past two weeks: walking for exercise, household chores, mowing and raking the lawn, gardening, hiking, jogging, biking, exercise cycle, dancing, aerobics, bowling, golf, single and double tennis, racquetball, calisthenics/weights, and swimming. Each activity was assigned a metabolic equivalent (MET) value allowing determination of total energy expenditure (Kcal/week) and energy expenditure (Kcal/week) in moderate/vigorous activities (≥ 4 METS).[2] In addition, the total time spent across all activities as well as moderate/vigorous activities was calculated. The self-reported PA values were averaged over the 14 days for comparison with the other PA devices.

3.2.7 **Statistical Analysis**

Statistical Package for the Social Sciences (SPSS, Chicago, IL; version 17) was used for this analysis. Distributions of all PA measures were inspected and for those not normally distributed square root transformation was applied. Analysis was done using both the raw data and the square root transformed variables to examine if results differed. To measure convergent validity (measurement of the agreement between tools that measure the same construct) Pearson product-moment correlations were computed to examine the association between the percentages of the recorded time spent in activities as measured by the five PA tools. Repeated measures analysis of variance (ANOVA) was used to determine whether the duration of activities was different across these tools. In addition, minute-by-minute values of accelerometer and HR monitor were correlated within each participant. Univariate relationships (Pearson product-moment correlations) between the FI and all PA measures were also considered. Participant scores for the FI were split into tertiles. Tertiles included the low FI (< 0.17), intermediate FI (0.17-0.38), and high FI (> 0.38). One-way (ANOVA) was performed to determine whether descriptive characteristics and PA measures differed across the three FI tertiles. Tukey post-hoc tests were run when there was a significant main effect for frailty. A significance level of $p \leq 0.05$ was set.

3.3 Results

3.3.1 Participation and Data Completeness

Accelerometer and HR monitor information were recorded for all 50 participants for 10 hours. No missing values were obtained for the accelerometer measures. Four participants had greater than 45% missing HR data over the 10 hours; their HR data were excluded from the analysis. There was ~ 3.8% of data missing from the remaining 46 participants with the high FI tertile (6.7%) having more missing values than the low FI tertile (0.4%; $p = 0.01$). Of these 46 participants, 31 were taking at least one medication that affects HR (e.g. beta blockers, calcium channel blockers, antiarrhythmics), thus their HRmax could not be estimated. The missing HR values were not different between participants who were on these medications and the others within the group ($p = 0.99$). Due to the limited battery life of the portable EMG device, approximately 9-9.5 hours of data were recorded. Therefore, all EMG data were truncated for analysis at nine hours. Complete EMG data over the nine hours were available from 37 participants for the VL and 39 participants for the BB. Two participants were excluded from the GPS data analysis because of insufficient data samples (< 2 hours). There were approximately 8.5 hours of data for the remaining 48 participants of which 94% of the GPS data points were recorded within 1 min of each other. The average duration between GPS data points were 22 seconds and the median times between data points was nine seconds. From these

48 participants, 28 had outdoor walking activity and two had vehicle travel activity. All 50 participants completed the MLTAQ.

3.3.2 **Distribution of PA Measures**

Most of the PA measures were positively skewed, except for; accelerometer total activity minutes, GPS speed and mean acceleration counts during outdoor activities, and the EMG number of bursts and total activity minutes for the BB. When square root-transformed data were used for these positively skewed variables results were either unchanged or very similar to the raw data analysis. The GPS and MLTAQ showed a floor effect with 20 (40% of all participants) and 14 participants (28% of all participants) scoring zero, respectively.

3.3.3 **Convergent Validity**

The minute-by-minute acceleration counts within each participant were positively correlated with the minute-by-minute step counts ($r = 0.76$-0.98; mean 0.92). This correlation was less ($p < 0.001$) in the high FI tertile ($r = 0.88$) compared with the low ($r = 0.95$) and intermediate FI tertile ($r = 0.93$). The minute-by-minute HR values within each participant were positively correlated with the minute-by-minute acceleration counts ($r = 0.27$-0.79; mean 0.58) and the minute-by-minute step counts ($r = 0.24$-0.78; mean 0.57). These correlations were not different across the tertiles ($p = 0.07$-0.14) and between the people who were taking medications that may influence HR and the remaining participants ($p = 0.10$-0.12)

The percentage of time spent in PA (amount of time within the testing period) measured by the accelerometer was significantly and positively correlated with the percentage of time spent in PA, as measured by GPS and MLTAQ and recorded EMG muscle activity (both in VL and BB). In addition, percentage of time spent in moderate/vigorous activity as measured with the accelerometer was significantly correlated with the MLTAQ (Table 3.1). The percentage of time spent in PA determined with accelerometers (31 ± 15%) and EMG muscle activity from the BB (30 ± 10%) was greater ($p \leq 0.05$) compared with the MLTAQ (23 ± 29%) and EMG of the VL (22 ± 10%). The percentage of time spent in PA measured with the HR monitors (36 ± 18%) was greater than all other tools, but not of statistical significance ($p = 0.05$-0.43). The percentage of time spent walking outdoors measured with the GPS (3 ± 6%) was less ($p < 0.001$) compared with the total activity measured by the other tools. The percentage of time spent in moderate/vigorous activities measured with the MLTAQ (4 ± 7%) was greater ($p < 0.001$) compared with the accelerometers (1 ± 2%). The percentage of time spent in moderate/vigorous activities measured with the HR monitors (3 ± 4%) was statistically similar ($p = 0.60$-0.73) to accelerometers and MLTAQ.

Table 3.1. Relationship Between Physical Activity Duration as Measured by Different Measurement Tools (Pearson Correlation Coefficient)

		Accel.	HR monitor	EMG (VL)	EMG (BB)	GPS
%time total physical activity	HR monitor	.255				
	EMG (VL)	.624†	.052			
	EMG (BB)	.326*	.417	.305		
	GPS	.497†	.194	.261	.274	
	MLTAQ	.529†	.203	.174	.240	.191
%time moderate/ vigorous activity	HR monitor	.162		N/A		
	MLTAQ	.523†	-.054			

Accel., Accelerometer; **HR**, Heart Rate; **EMG**, Electromyography; **VL**, Vastus Lateralis; **BB**, Biceps Brachii; **GPS**, global positioning system; **MLTAQ**, Minnesota Leisure Time Activity Questionnaire $^{*}p \leq 0.05$; $^{\dagger}p \leq 0.01$

3.3.4 Relation Between Frailty and Physical Activity Measures

The FI was significantly correlated to all accelerometer and MLTAQ measures and the number of bursts for VL and BB. No correlation was found between the FI and the HR monitor measures. The participants who remained indoors for all 10 hours (FI = 0.34) had greater (p = 0.05) FI than the participants who had some outdoor PA (FI = 0.24). In these participants who had some outdoor PA the GPS speed was significantly (p = 0.04) correlated with the FI. The PA measures that were the most closely related to FI were the number of steps and the minutes spent in PA as measured by the accelerometer (Table 3.2).

Table 3.2. Relationship Between Frailty Index and Physical Activity Measures (Pearson Correlation Coefficient)

		Frailty Index
Accelerometer	Total steps	$-0.644^{\dagger}$
	Total acceleration counts	$-0.584^{\dagger}$
	Acceleration counts/min during activity	$-0.441^{\dagger}$
	Total activity minutes	$-0.617^{\dagger}$
	Moderate/Vigorous activity minutes	$-0.483^{\dagger}$
EMG	Number of bursts (VL)	-0.367^{*}
	Number of bursts (BB)	-0.336^{*}
GPS	Speed	-0.386^{*}
Questionnaire	Total activity kcal/week	$-0.607^{\dagger}$
	Moderate/Vigorous activity kcal/week	$-0.562^{\dagger}$
	Total activity minutes	$-0.603^{\dagger}$
	Moderate/Vigorous activity minutes	$-0.562^{\dagger}$

EMG, Electromyography; **VL**, Vastus Lateralis; **BB**, Biceps Brachii; **GPS**, global positioning system $^{*}p \leq 0.05$; $^{\dagger}p \leq 0.01$

3.3.5 Physical Activity Measures Across Tertiles of Frailty

Height, weight, and number of medications were similar among the three FI tertiles. High FI women were older than the other two tertiles and had more comorbidities and falls than the low FI women. In contrast, no difference was found in number of comorbidities and falls between the low and intermediate FI women (Table 3.3). Univariate tests demonstrated a significant main effect of frailty on all PA variables measured with accelerometers and MLTAQ and on the number of bursts for the VL as measured with EMG. For these significant main effects, post-hoc testing revealed that the high FI group scored lower on these PA measures compared to the low FI group. High FI women had fewer steps and PA minutes and scored lower on all MLTAQ measures as compared with the intermediate FI women. The intermediate FI tertile scored lower on all PA variables measured with the accelerometers and MLTAQ (except the mean acceleration counts per minute of PA) as compared with the low FI tertile. Eleven of the 17 high FI women (65% of all participants) scored zero on all MLTAQ measures. The PA variables measured with HR monitors and GPS were different across frailty tertiles but these differences did not reach significance. Only two high FI women were free of medications that might influence HR, thus estimates of PA intensity based on HRR were limited. Six of the high FI women had some outdoor activity to estimate speed and acceleration activity counts during outdoor activities (Table 3.3).

Table 3.3. Descriptive Characteristics and Physical Activity Measures Across FI tertiles

		Low FI		Intermediate FI		High FI	
		N	Mean±SD	**N**	Mean±SD	**N**	Mean±SD
Descriptive	Age (years)	16	71 ± 4	17	75 ± 5	17	81 ± 6*†
	Height (cm)	16	154 ± 4.8	17	155 ± 5.6	17	152 ± 7.1
	Weight (kg)	16	68.2 ± 9.6	17	77.7 ± 11.2	17	73.9 ± 16.6
	# Self-reported Comorbidities	16	1.6 ± 1.0	17	2.8 ± 1.6	17	3.3 ± 1.9*
	# Prescription Medication(s)	16	4.2 ± 2.4	17	5.1 ± 2.9	17	5.5 ± 3.3
	# Fall(s)	16	0.5 ± 0.7	17	1.7 ± 1.9	17	2.8 ± 3.5*
Accelerometer	Total steps	16	3599 ± 1781	17	1773 ± 1048*	17	873 ± 809*†
	Total acceleration counts	16	91797 ± 41952	17	51497 ± 32808*	17	28969 ± 24454*
	Total activity acceleration counts/min	16	340 ± 142	17	249 ± 106	17	210 ± 104*
	Total activity minutes	16	259.8 ± 78.8	17	179.7 ± 58.3*	17	117.1 ± 67.7*†
	Moderate/Vigorous activity minutes	16	11.5 ± 14.2	17	4.4 ± 7.0*	17	2.1 ± 4.5*
HR monitor	Total activity minutes	7	238.3 ± 120.0	6	215.0 ± 101.1	2	166.2 ± 84.6
	Moderate/Vigorous activity minutes	7	20.0 ± 23.9	6	18.5±29.8	2	6.0 ± 4.2

(Table 3.3 continued pg.59)

Table 3.3. (Continued)

		Low FI		Intermediate FI		High FI	
		N	Mean±SD	**N**	Mean±SD	**N**	Mean±SD
EMG	# bursts (VL)	11	10825 ± 4669	11	8351 ± 2744	15	6731 ± 3711[*]
	# bursts (BB)	12	12177 ± 2710	12	10897 ± 1486	15	10222 ± 2956
	Total activity minutes (VL)	11	135.4 ± 70.8	11	120.2 ± 36.7	15	103.0 ± 52.7
	Total activity minutes (BB)	12	163.2 ± 53.4	12	159.8 ± 59.0	15	167.0 ± 58.1
GPS	Outdoors activity minutes	16	27.3 ± 45.6	17	13.4 ± 19.7	15	8.2 ± 13.7
	Outdoor activity distance (meters)	16	870.1 ± 1372.3	17	376.3 ± 424.5	15	334.6 ± 578.3
	Outdoor Activity speed (m/sec)	13	0.92 ± 0.21	9	0.88 ± 0.23	6	0.69 ± 0.24
	Outdoor activity acceleration counts/min	13	551 ± 228	9	419 ± 268	6	333 ± 273
MLTAQ	Total activity kcal/week	16	6092 ± 4167	17	3551 ± 4988[*]	17	1008 ± 1921[*†]
	Moderate/Vigorous activity kcal/week	16	1321 ± 1157	17	684 ± 1393[*]	17	81 ± 292[*†]
	Total activity minutes	16	241.9 ± 166.5	17	141.5 ± 198.6[*]	17	40.7 ± 77.3[*†]
	Moderate/Vigorous activity minutes	16	47.2 ± 41.3	17	24.4 ± 49.8[*]	17	2.9 ± 10.4[*†]

FI, Frailty Index; **HR**, Heart Rate; **EMG**, Electromyography; **VL**, Vastus Lateralis; **BB**, Biceps Brachii; **GPS**, global positioning system; **MLTAQ**, Minnesota Leisure Time Activity Questionnaire
[*]Significantly different from the low FI tertile; [†]Significantly different from the intermediate FI tertile

3.4 Discussion

The association of frailty with level of PA measured using multiple objective and self-reported methods was examined in 50 older women from rural Greece. To our knowledge this is the only study that has used multiple tools to quantify PA in older women across levels of frailty. The main outcome of this study was that convergent validity was strong between accelerometers and the other PA measures (EMG, GPS, MLTAQ) but weaker when the other measures were compared among each other. Number of steps and duration of activity measured with accelerometers were more strongly related to frailty than the other measures. The PA measures that were significantly different between tertiles were those measured with accelerometers and the MLTAQ, but MLTAQ had a large floor effect for the older women within the high FI tertile.

Similar to our study, other reports correlate self-reported PA with objective measures of PA in older adults,[13,14,17] but objective measures were more strongly associated with health status.[14] Time spent in total activity ranged from 2.2-3.5 hours and time spent in moderate/vigorous activity ranged from 6-24 minutes. To our knowledge no other study has examined PA in Greek older adults using objective measures. Studies using self-reported questionnaires were in agreement with our study that total and moderate/vigorous PA in Greece is quite low. In the ATTICA study 38% of Greek women above the age of 60 were physically active.[29] In another study, 21% of Greek women above the age of 70 responded that they participated 1-4 times per week in PA outside of sports (e.g. walking, gardening) and only 2% responded as regular exercise participants.[30] In the Pan-EU study, 71% of European women above the age of 65 spent less than 10% of their energy expenditure in moderate/vigorous activities and Greece had one of the lowest prevalence rates of moderate/vigorous activities compared with the other European countries.[31] The level of PA of Greek rural older women in this convenience sample may not be representative of the level of PA of Greek older women living in cities which is speculated to be even lower.[29]

The total step and acceleration counts in this study were approximately half of that previously reported, even for those within the low FI tertile.[14,20,32] However, we recorded PA for 10-daily hours compared with other studies that examined PA over the full awake hours throughout a day. The mean acceleration counts per minute in community-dwelling Greek older women of this study were 48-153. The low FI tertile activity counts (153 counts/min) were similar to those found in community-dwelling US older women above the age of 70 (170 counts/min)[9] but less than those found in active healthy Canadian older women (294 counts/min)[13] and slightly greater than those reported for US older women at risk for mobility disability (132 counts/min)[17] and those residing in a nursing home (20-102 counts/min).[15] These differences are not surprising since we showed that mean acceleration counts declined with advanced frailty making comparison between studies erroneous if the frailty level was dissimilar. The mean acceleration count during walking at a speed of 0.9 m/sec in older women is ~ 273 counts/minute.[15] During the active periods in our study accelerometer counts were 210-340 and walking at a usual pace was 0.9 m/sec. This result illustrates that the older women in this study spent most of their active time walking. The GPS speed found in a previous study[20] in older adults was 1.27 m/sec which is greater than the GPS speed found in this study even for the low FI tertile (0.92 m/sec); however, in our study we did not exclude participants who walked less than 10 minutes consecutively outdoors which presumably the other study did.[20]

EMG provides an indication of when a muscle is active or resting[23] and enables determination of the duration of time spent in low, moderate, and high levels of muscle activity relative to maximum.[22] In this study we found that EMG activity of the upper and lower body was correlated with the FI and the PA measured with accelerometers. Also, the percentage of time in which the muscles were active was similar to the percentage of PA accumulated throughout the day. Muscle activity of the upper body relative to the lower body had longer burst durations most likely because older women spend a greater portion of the day seated or standing while they were doing housework. Many PA measures are not sensitive to this accumulation of PA. EMG is not meant to be a measurement tool for PA, but when low-threshold EMG bursts are calculated and used in combination with measures of gross movement such as accelerometers it likely supplies important information about upper body movements that cannot be gained from traditional whole body assessment. Ultimately, it offers a means to determine how hard the muscle is working while performing PA.

The duration of moderate/vigorous PA measured with accelerometers was correlated with self-reported PA duration despite self-reported PA duration being 3% longer. This is not surprising since most self-reports overestimate duration and intensity of PA, especially for moderate PA.[33] The moderate/vigorous PA minutes measured in this study with accelerometers were similar to those measured with the same device in US community-dwelling older women (6 min/day).[9] There were large, but non-significant, differences in time spent in PA between frailty tertiles when HR monitors were used to define intensity. This lack of statistical significance may be explained by the large variance seen in all PA measures and the smaller sample included for HR recordings.

The current recommendation of a minimum of 30 minutes of moderate PA[12] was only achieved by; one woman as measured by accelerometer, four women as measured by HR monitor, and 13 women when a self-report questionnaire was used as the measurement tool. Harris et al.[32] also found that when PA was recorded with accelerometers only 2.5% of the older adults (6/238) achieved the recommended level of PA. Recommended levels of PA are based primarily on self-report rather than accelerometers and adherence to these recommendations is substantially lower when accelerometers are used as the measurement tool relative to self-report.[9] Thus, the recommended duration and intensity of PA to improve health is likely lower if accelerometers are to be used as an assessment tool.

The moderate/vigorous intensity outcomes must be interpreted with caution. Cut-off values to assess the time spent in different intensities of PA are unknown for frail older adults for any of the devices used in this study. Accordingly, we used the cut-off values proposed for healthy older adults. For example, 4 METS was the cut-off for moderate intensity for the MLTAQ[2], but 4 METS may be perceived as a light activity for healthy and very active older adults, but vigorous activity for a frail person. Thus, the duration of time spent in moderate activities for frail women in this study is likely underestimated. However, a recent study[16] found that the cut-off values for moderate activity measured with accelerometers are similar between young (20-29 years), middle-aged (40-49) and older healthy adults (60-69 years). This finding suggests that there might be no need to create different cut-off values based on age. Future research should examine whether the current recommendations for PA in older adults are applicable for frail older adults and whether the type, intensity and time (net acquisition over day or single bout) of PA is relevant for this population in order to improve health and fitness.

Self-report PA is relative easy to measure, but influenced by fluctuations in health status, depression, fatigue and cognitive ability which are all common issues in frail older adults.[34] Activities that are most difficult to recall are the light to moderate activities,[35] which are typically most relevant in frail adults. In addition, walking which is the most important activity to measure in this population, is unreliably assessed by questionnaire.[36] PA questionnaires designed for healthy older adults may be inaccurate when used with frail adults. The short version of the MLTAQ, used in this study, was not validated for older adults but was used for the development of the frailty phenotype in the Cardiovascular Health Study and subsequently used extensively for the measurement of PA in frail older adults.[3] The original MLTAQ was designed for a young population, is generalizable to men only, and valid for healthy older adults but mostly for the measurement of moderate intensity activities.[37] This questionnaire tends to focus more on moderate to vigorous activities,[19] illustrated through the large floor effect observed in the high FI group. Although this questionnaire is regularly used it may not be valid for the measurement of PA in frail adults. The Stanford 7-day Physical Activity Recall questionnaire likely offers greater representation of PA in frail older adults.[19,37] Research is needed to examine which PA questionnaire is most appropriate for frail older adults and establish an effective recall period (days, weeks, months) that may best suit this population.

Waist-mounted accelerometers underestimate upper body movements but HR monitors and EMG devices could overcome this problem. Actigraph accelerometer measured step counts have been shown to be accurate for walking speeds above 0.9 m/s but less accurate for lower speeds.[20,38] Therefore the steps recorded in this study may be underestimated, especially for the frail older women. Recording step counts with accelerometers is more accurate than pedometers for slower speeds and shorter distances.[38] HR monitors overestimate light activity,[27] which is common in older adults and especially in frail older adults, and is influenced by factors such as temperature, emotional state, caffeine etc.[39] In addition, prescription medications would likely alter heart rate, thus known equations to estimate HRmax could not be used. However, the HR values within each participant were positively correlated with the accelerometer data regardless of medication use, thus these devices might be limited for exact estimation of HRmax, but useful for determination of overall PA level. Future studies should directly measure maximal exercise values for each individual and then HR monitors may be used to establish the percentage of exercise intensity relative to HRmax. The lower correlation of HR with accelerometer values within each participant compared with the correlation of step counts with acceleration counts can be explained by the fact that HR takes a few minutes to decline after the termination of an activity.[18]

It is recommended that older adults wear PA devices for a minimum of three days and encompass weekdays and weekends to enhance accuracy of measurement;[40] however, some devices like GPS have limited time-logging and allow less than nine hours recording. Frail older adults are less active and may have less variance in their activities across days;[13] thus, future research should not only examine the appropriate device but also the recording period. The self-report questionnaire provided information on the type of PA performed and the GPS established if the PA was done outside, but all other objective measures could not provide information on the type of PA performed by these older women. Ongoing surveillance, either by shadowing the person or by video camera, could objectively measure types of PA but both methods have ethical and practical limitations in that they might influence task performance and daily life PA habits.

Each PA measurement tool has limitations and may measure different aspects of PA, thus one independent method may not offer a gold standard. Accelerometers record upright physical activity, EMG measures muscle activity, heart rate monitors estimate physiological response to PA, and GPS quantifies outdoor PA. A combination of these methods may overcome independent limitations and provide important information about the level of PA in older women across levels of frailty. In addition, combining these methods in a single device with sensors in upper and lower body and trunk would simplify the synchronization of the data, reduce the cost of buying multiple devices, and improve the prediction of the intensity of the PA.[39]

This study examined the use of five different methods to measure PA in older women across levels of frailty. Accelerometers showed good agreement with the other PA methods, had the strongest association with frailty, and could be used to dissociate levels of frailty. Each method examined in this study had limitations but provided useful information about different aspects of PA in this population. Multiple methods can be used to accurately determine the duration and intensity of PA in older adults across levels of frailty.

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CHAPTER 4

Daily Muscle Activity and Quiescence in Non-Frail, Pre-Frail, and Frail older women[a]

4.1 Introduction

Research into frailty has recently become a key focus of gerontology research. Knowledge surrounding this geriatric syndrome within the past decade has increased exponentially.[1] Frailty is often defined as a state of vulnerability caused by cumulative declines across multiple physiological systems resulting in adverse health outcomes (falls, disability, hospitalization, institutionalization) or death. The criteria used for identification of frail persons continue to be a matter of debate; however, the most commonly used approaches to qualify older adults with this syndrome are the Frailty Phenotype[2] and the Frailty Index[3]. While frailty often culminates in the need for institutional care,[4] many frail older adults still remain in the community despite impairments in one or more activities of daily living (ADL).[5] This syndrome is more common in women than men. Age-related decline of muscle mass and strength will likely cause women to transition into frailty sooner than men.[2] In addition, there are differences in the prevalence of frailty between countries and races.[6] The majority of frailty studies have been conducted in North America, but recent studies suggest that frailty may be more prevalent in Europe possibly due to social and environmental factors.[7-9] For example, in Greece which has one of the oldest populations in Europe (19.2% of population over 65 years of age),[10] the prevalence of frailty and pre-frailty in community-dwelling older adults over 65 years of age were 15% and 45%, respectively.[9]

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Reduced muscle mass, strength, and motor control are likely fundamental components of frailty, yet a cause and effect relationship has not been established. Consequences of these changes in frail people are increased rates of falls, fractures and disability.[11] Frail older adults have reduced muscle mass and strength and greater fat mass than non-frail older adults.[7] Fried et al.[2] utilized low isometric handgrip strength as an indicator of frailty. While handgrip has been proposed as a good predictor of health related events[12] it only measures upper limb strength and may not entirely capture the function of the lower extremities[7] which seemingly are key to loss of mobility. Impaired motor control and slowed gait speed are readily observed in frail older adults.[13] To our knowledge, no investigation has yet examined if frailty is associated with differential changes in muscle activity based upon anatomical location (upper or lower body) or functional movement (flexion, extension). It is well established that general age-related change is not similar across all muscles[14-17] and therefore various muscles may need to be considered when examining changes in muscle function in frail older adults. In addition, physical activity levels should also be considered. Physical activity interacts with the natural process of aging and is known to alter the rate of age-related progressive decline in muscle function.[18]

Muscle activity and quiescence, termed low-threshold electromyography (EMG), was recently used to examine muscle function in healthy community-living older adults,[19] as well as younger adults to understand work-related injuries.[20-24] No studies have yet examined EMG during daily life in frail persons. Daily activities are often reported to be “hard work” for most frail adults, and often this ‘work’ results in falls and injuries. Measuring muscle activity during daily life may elucidate our understanding of progressive functional decline as well as acute adverse events such as falls in frail older adults. In addition, daily upper and lower limb muscle activity and quiescence is a result of an interaction of several systems (e.g. muscular and nervous system) and may be a more complete indicator of health than handgrip strength. Therefore, these variables are likely to be more precise indicators of frailty. Given the syndromic characteristic of this condition, we acknowledge that a combination of various frailty indicators, in addition to daily muscle activity and quiescence, are likely needed to make a complete clinical diagnosis of frailty.

Laboratory and functional performance measures are important, but limited for this population. Most laboratory tests developed for older adults are not applicable to frail adults and often frail older adults are unable to attend a laboratory for testing due to their impaired health. Measurements that will capture the daily life of the frail person in the home environment are needed. Recent studies measuring muscle activity during daily life and discrete tasks reported muscle activity was greater in non-frail older adults relative to young adults. In addition, this age-related difference was greater in women compared with men.[19,25] Muscle activity and quiescence recorded during daily life in older women across various stages of frailty is unknown, but could contribute to our understanding of the progression of this syndrome. The purpose of this study was to determine whether muscle activity and quiescence recorded over a 9-hour typical day in upper and lower limb muscles differs between non-frail, pre-frail and frail older women. Due to known sex differences in the development of frailty,[2] women were studied to investigate our hypothesis that upper limb muscle activity would be greater than that recorded in the lower limb and that muscle activity would increase across stages of frailty.

4.2 Methods

A convenience sample of 33 community-dwelling women aged 68-90 years who were living in rural areas within the prefecture of Thessaloniki, Greece participated in this study. Inclusion criteria were women older than 65 years of age who were living in the local community. The study was approved by the University of Western Ontario Ethics Board and informed consent was received prior to participation.

During weekdays the researcher visited the home of the participants twice. The first visit entailed administration of a health history questionnaire, determination of frailty using the frailty phenotype[2] and a measurement of muscle strength. The following day the researcher arrived approximately one hour after the participant awoke. An EMG device and accelerometer were attached to the participant and Maximal Voluntary Exertions (MVE) for each muscle of interest were performed. Participants were then instructed to proceed with their normal daily activities while wearing the portable EMG and accelerometer. Participants were also asked not to bathe or exercise vigorously in order to prevent dislodging the electrodes and damage to the recording device. The researcher encouraged participants to disregard the equipment and undertake a typical day. Approximately 9-10 hours later the researcher returned to the participant's home to remove the equipment.

4.2.1 Frailty Definition

Physical frailty was defined using the frailty phenotype as described in the Cardiovascular Health Study.[2] The five frailty criteria were measured as outlined below.

If participants did not score/respond within the predetermined cut-off measure, they received one point. When three or more criteria were attained, a state of frailty was defined. One or two criteria were scored as pre-frailty and zero as non-frailty.

1) Weight loss: A positive response to the question "In the last year, have you lost more than 5 kg unintentionally (i.e., not due to dieting or exercise).
2) Muscle strength: The highest of three consecutive maximal handgrip strength measures of the dominant hand using a Jamar® hand-held dynamometer. Cut-off scores were applied based upon body mass index (BMI ≤ 23, cut-off strength ≤ 17kg; BMI 23.1–26, cut-off strength ≤ 17.3kg; BMI 26.1–29 cut-off strength ≤ 18kg; BMI > 29 cut-off strength ≤ 21kg).
3) Walking speed: Time to walk 15 feet at usual pace. Cut-off scores were applied based upon height (Height ≤ 159 cm, cut-off time ≥ 7 sec; Height > 159cm, cut-off time ≥ 6 sec).
4) Physical activity: A weighted score of kilocalories expended per week was calculated based on participant's responses to the Short version of the Minnesota Leisure Time Activity Questionnaire (cut-off < 270 Kcals per week).
5) Subjective fatigue: Responding to the questions "How often in the last week did you feel that everything you did was an effort?" or "How often in the last week did you feel that you could not get going?" either moderate amount of the time or most of the time.

4.2.2 **Electromyography**

Muscle activity and quiescence were measured with a portable surface EMG device (Biometrics DataLOG P3X8, Gwent, UK). Details of the EMG data collection and analysis are described elsewhere.[19,25] Briefly, surface electrodes were placed mid-belly of two major arm muscles [biceps brachii (BB), triceps brachii (TB)] and two major thigh muscles [vastus lateralis (VL), and biceps femoris (BF)] on the self-reported dominant side. A common ground electrode was placed on the lateral malleolus of the fibula. The inter-electrode distance was fixed at 20 mm and the EMG data logger (9.5 x 15.8 x 3.3 cm; 380 gram) was secured to a belt worn at the waist. The signal from the electrodes was sampled at 1,000 Hz, amplified (1,000x), band-pass filtered (20-450 Hz), and stored on a 512 MB MMC flashcard.

Subsequent to EMG electrode placement and setup of the recording unit isometric maximal voluntary exertions (MVE) were performed for the four muscles (VL, BF, BB, TB) in order to normalize the 9-hour EMG recordings to a percentage of the participant's maximum. The MVE were recorded in a seated position during isometric knee and elbow extension and flexion against resistance provided manually by the researcher. The knee and elbow joint were bent to ~ 90° during the MVE of the thigh and arm muscles, respectively. Each muscle was tested in a randomized order three times with 60 seconds rest between trials. The greatest of the three trials was used for normalization of the 9-hour EMG data. Verbal encouragement was provided by the researcher to ensure maximal effort.

All EMG data during the MVE and the 9-hour testing were imported into Biometrics software (Biometrics DataLog version 3, Gwent, UK) for preliminary visual inspection and subsequently into Spike 2 Version 5 (Cambridge Electronics Design, Cambridge, UK) for analysis using custom script software. Data artefacts (~ 5% of the total time) were manually removed across all four channels in a time-locked fashion.

Signals were rectified, smoothed at a time constant of 0.01 seconds and down-sampled by a factor of 100. Bursts and gaps in the EMG signal were computed to quantify muscle activity and quiescence during the 9-hour testing period. Bursts, which represent muscle activation, were defined as a period of EMG activity greater than 2% of MVE for a duration longer than 0.1 second. Burst characteristics examined were; number of bursts, mean duration (seconds), burst percentage (% of total recording time occupied by bursts), peak amplitude (average peak amplitude of all bursts, %MVE), and mean amplitude (average mean amplitude of all bursts, %MVE). Gaps, which represent muscle quiescence, were quantified as a period of EMG less than 1% of MVE for a duration longer than 0.1 seconds. Gap characteristics examined were; number of gaps, mean duration (seconds), gap percentage (% of total recording time occupied by gaps). Previous research has used burst and gap analysis to quantify muscle activity and quiescence.[19,20,23,25-28]

4.2.3 **Mobility**

Mobility during the nine hours of testing was measured using the ActiTrainer accelerometer (Actigraph, LLC, Fort Walton Beach, FL). The ActiTrainer (8.6 x 3.3 x 1.5 cm; 51 grams) is a uniaxial accelerometer that was programmed to record data in 1-minute epochs. It was secured in a holster, attached to a belt, which was worn at the waist on the dominant side parallel to the mid-axillary line. Actitrainer data was downloaded into the ActiLife software (Actigraph, LLC, Fort Walton Beach, FL) and step-counts per minute were used to calculate the number of steps completed by the participants during the 9-hour testing.

4.2.4 Muscle Strength

Maximal isotonic knee extension strength of the dominant leg was measured using the adjustable Recordman™ foot weights and one repetition maximum with the participant seated in a chair with the knee bent to ~ 90°. Initially, participants performed three submaximal knee extensions with a light load foot weight (~ 2-3 kg) to warm-up. Participants performed a series of single repetition lifts with increasing weight loads until a one repetition maximum (1RM) lift was achieved in approximately 3-5 attempts. 1RM was defined as the maximal weight that the participants could lift safely through the full range of motion.[29]

4.2.5 Statistical Analysis

The Statistical Package for the Social Sciences (SPSS, Chicago, IL) for Windows version 16.0 was used for statistical analysis. Repeated measures multivariate analysis of variance (MANOVA) was performed to determine the effect of frailty and muscle on muscle activity and quiescence. Frailty (non-frail, pre-frail, frail) was the between-subject independent variable and muscle (VL, BF, BB, TB) was the within-subject independent variable. The dependent variables were the five burst (number of bursts, mean duration, burst percentage, peak amplitude, mean amplitude) and three gap characteristics (number of gaps, mean duration, gap percentage) which indicated muscle activity and quiescence, respectively. One-way analysis of variance (ANOVA) was performed to determine whether participants' characteristics (age, height, weight, number of comorbidities and medications, history of falls, muscle strength, mobility) differed between the three frailty groups. Pair-wise comparisons were conducted when there was a significant main effect of frailty and/or muscle on the dependent variables. Pearson's product-moment correlations were computed to examine the association between mobility and muscle activity and quiescence of the two thigh muscles. A significance level of $p \leq 0.05$ was accepted. Data in the text and table are reported as values ± standard deviation of the mean, whereas figures are presented as values ± standard error of the mean.

4.3 Results

Ten women were categorized as non-frail, 11 as pre-frail, and 12 as frail (Table 4.1). Height, weight, number of self-reported comorbidities, number of medications, and number of falls within the past year were similar among the three groups ($p > 0.05$). Frail women were older, had weaker leg extension strength, and walked fewer steps during the 9-hour testing period compared with the pre-frail and non-frail women ($p < 0.05$). In contrast, no differences were found in age, leg extension muscle strength, and mobility between non-frail and pre-frail women ($p > 0.05$) (Table 4.1). The two way interaction of frailty by muscle was non-significant for both burst ($p = 0.06$) and gap activity ($p = 0.96$).

Table 4.1. Descriptive Characteristics

	Non-frail (n=10)	Pre-frail (n=11)	Frail (n=12)
Age (years)	74 ± 4	75 ± 4	81 ± 6*
Height (cm)	155 ± 6.0	156 ± 4.8	150 ± 7.5
Weight (kg)	65.7 ± 8.4	77.8 ± 16.2	71.7 ± 13.4
Number of Self-Reported Comorbidities	1.8 ± 1.3	2.4 ± 1.8	3.4 ± 2.0
Number of Prescription Medication(s)	4.4 ± 3.0	3.6 ± 2.8	6.2 ± 3.1
Number of Falls in the Past Year	0.9 ± 1.7	1.7 ± 3.1	1.9 ± 2.4
Number of Steps in Nine Hours	3147 ± 2031	2094 ± 1087	481 ± 394*
Isotonic Leg extension Strength (kg)	10.0 ± 2.3	8.7 ± 2.7	6.2 ± 1.5*

*Significantly different from non-frail and pre-frail
cm, centimeters; **kg**, kilograms
$p \leq 0.05$

4.3.1 **Frailty**

A significant ($p = 0.001$) multivariate main effect of frailty on burst activity across all muscles was found. Univariate tests demonstrated a significant ($p < 0.05$) main effect of frailty on three of the burst characteristics (number of bursts, mean burst duration, and mean burst amplitude). Burst percentage (Figure 4.1A) and peak amplitude (non-frail 8.8 ± 3.0, pre-frail 8.8 ± 2.1, frail 7.7 ± 2.4 %MVE) were similar ($p > 0.05$) across all frailty groups. Post-hoc testing revealed that the number of bursts was less ($p = 0.01$) in the frail than the non-frail women, and pre-frail women did not differ from non-frail or frail (Figure 4.1B). Mean burst duration was greater ($p < 0.05$) in frail and pre-frail than in the non-frail women; however, there was no difference ($p = 0.73$) between the pre-frail and frail women (Figure 4.1C). Mean burst amplitude was greater ($p < 0.05$) in the pre-frail women than the non-frail and frail women. No difference ($p = 0.54$) was found in the mean burst amplitude between the frail and non-frail women (Figure 4.1D).

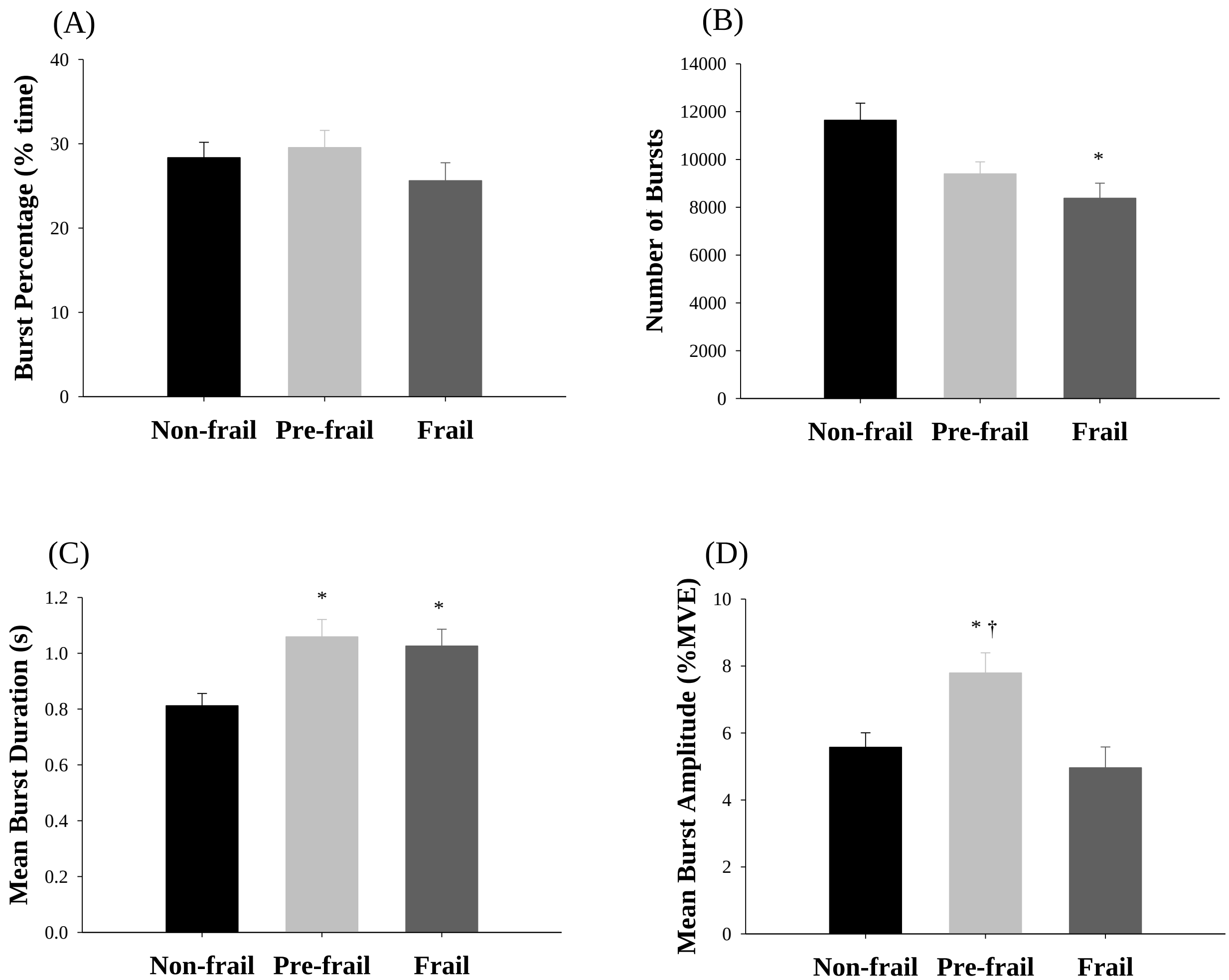

Figure 4.1. Burst Activity for Non-Frail, Pre-Frail, and Frail Women
(A) Burst percentage; (B) Number of bursts; (C) Mean burst duration; (D) Mean burst amplitude
%, percentage; **s**, seconds; **MVE**, maximal voluntary exertion
[*]Significantly different from non-frail women; [†]Significantly different from frail women
$p \leq 0.05$

A significant ($p = 0.01$) multivariate main effect of frailty on gap activity across all muscles was found. Univariate tests demonstrated a significant ($p < 0.05$) main effect of frailty on number and mean duration of gaps. The gap percentage was similar ($p = 0.91$) across all frailty groups (Figure 4.2A). Post-hoc testing revealed that the number of gaps was greater ($p < 0.01$) in the frail than the non-frail and pre-frail women; however, there was no difference between the non-frail and pre-frail women (Figure 4.2B). Mean gap duration was less ($p = 0.01$) in the frail than the pre-frail women. In contrast, no difference ($p > 0.05$) was found in the mean gap duration of the non-frail women compared with the pre-frail and frail women (Figure 4.2C).

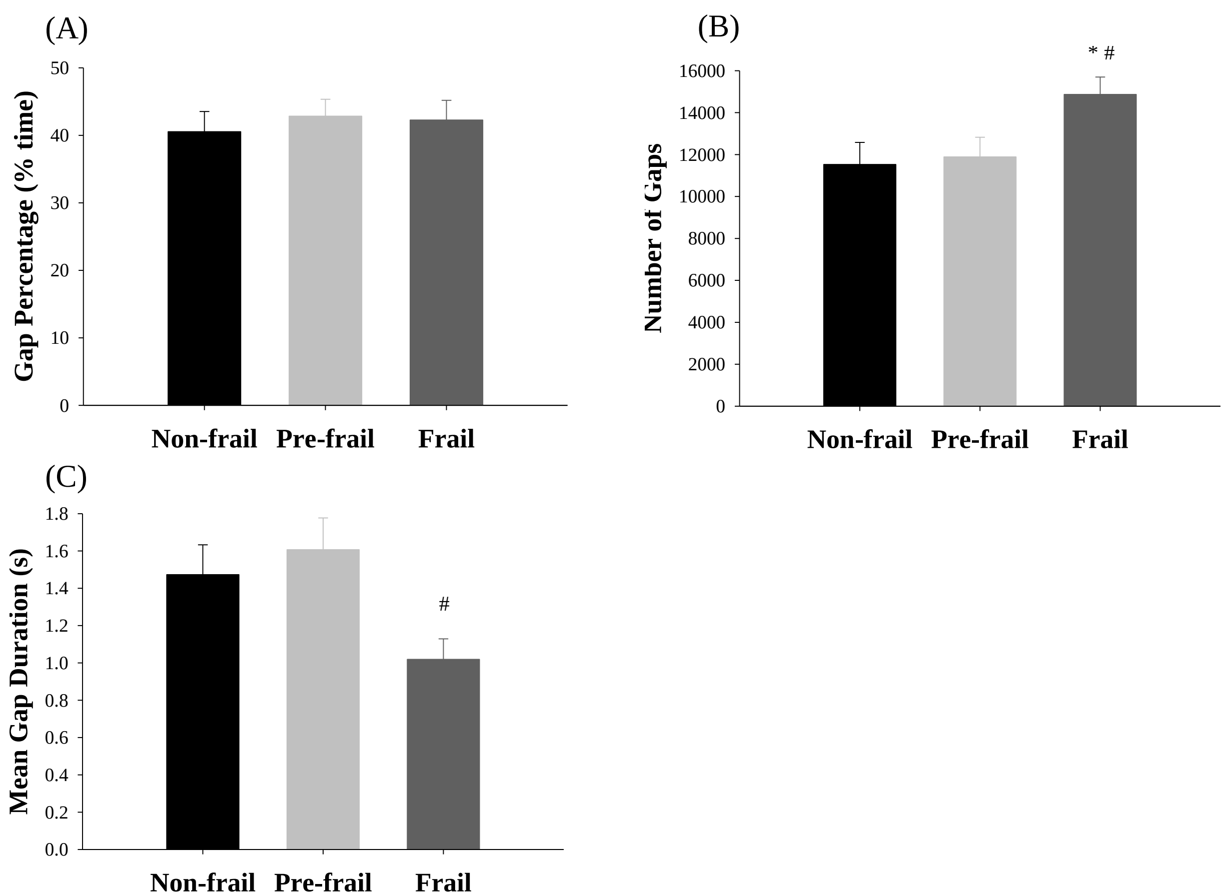

Figure 4.2. Gap activity for Non-Frail, Pre-Frail, and Frail women
(A) Gap percentage; (B) Number of gaps; (C) Mean gap duration
%, percentage; **s**, seconds
*Significantly different from non-frail women; #Significantly different from pre-frail women
$p \leq 0.05$

4.3.2 **Muscles**

A significant ($p < 0.001$) multivariate main effect of muscle on burst activity across all frailty groups was found. Univariate tests demonstrated a significant ($p < 0.05$) main effect of muscle on all burst characteristics. Pair-wise comparisons revealed that the burst percentage was greater ($p \leq 0.01$) in both of the arm muscles (BB and TB) compared with the two thigh muscles (VL and BF). In addition, burst percentage was greater ($p < 0.001$) in the TB than the BB; however, there was no difference ($p = 0.19$) between the VL and BF (Figure 4.3A). The number of bursts was greater ($p < 0.001$) in the arm muscles (BB and TB) than the thigh muscles (VL and BF); however, there was no difference between the VL and BF and between the BB and TB (Figure 4.3B). Mean burst duration was greater ($p < 0.05$) in the TB compared with the VL and BB (Figure 4.3C). Peak burst amplitude was less ($p < 0.01$) in the BB compared with the other three muscles, and the BF was greater ($p < 0.05$) than the VL and TB (Figure 4.3D). Mean burst amplitude was greater ($p < 0.05$) in the TB compared with the other 3 muscles (Figure 4.3E).

A significant ($p < 0.001$) multivariate main effect of muscle on gap activity across all frailty groups was found. Univariate tests demonstrated a significant ($p < 0.001$) main effect of muscle on all gap characteristics. Pair-wise comparisons revealed that the gap percentage was less ($p < 0.01$) in the TB compared with the other three muscles and in the BB compared with the BF (Figure 4.4A). The number of gaps was less ($p < 0.01$) in the BB compared with the other three muscles and in the TB compared with the BF (Figure 4.4B). Mean gap duration was greater ($p < 0.05$) in the BB compared with the other three muscles and in the VL compared with the TB (Figure 4.4C).

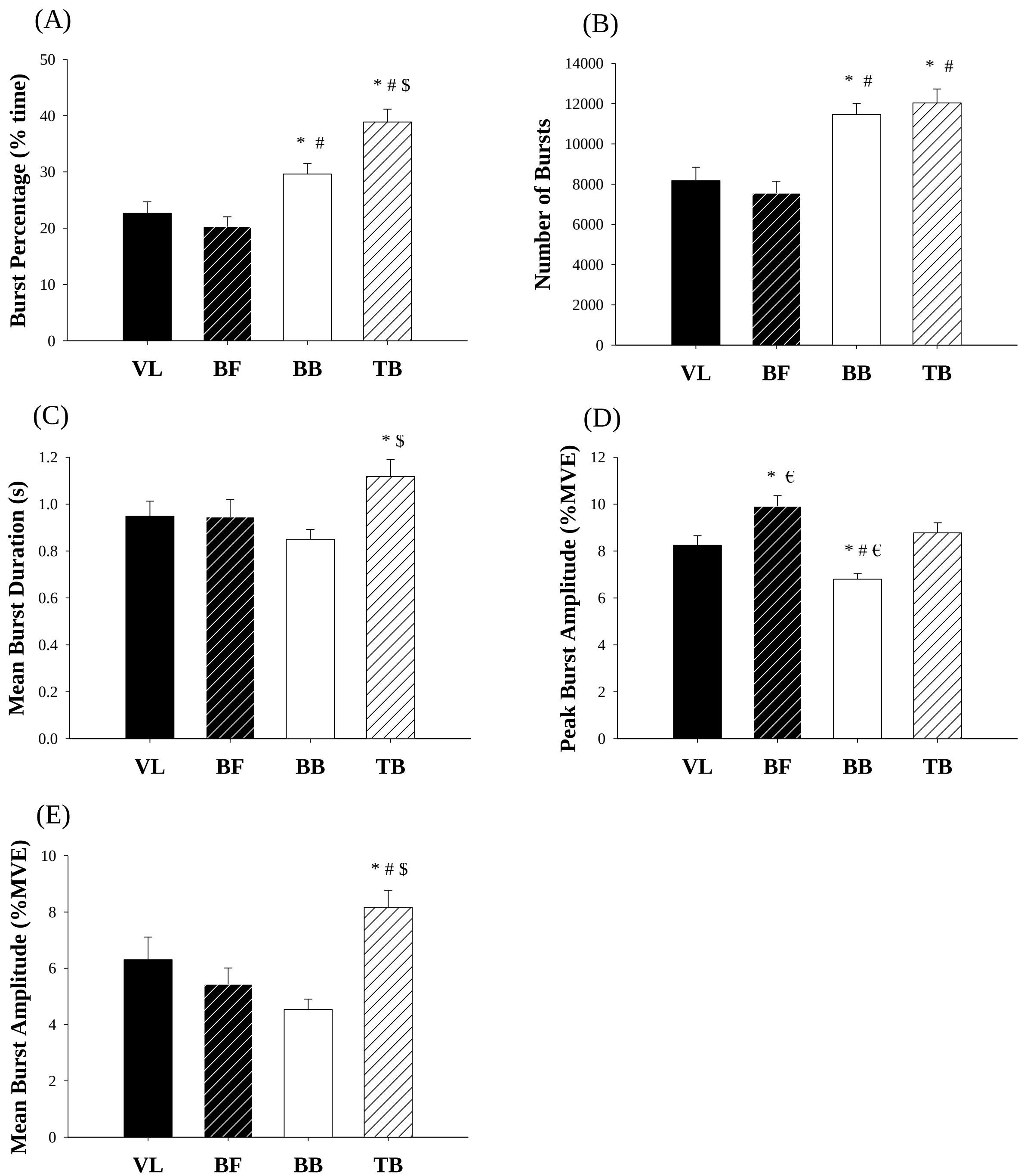

Figure 4.3. Burst Activity for the Vastus Lateralis, Biceps Femoris, Biceps Brachii, and Triceps Brachii

(A) Burst percentage; (B) Number of bursts; (C) Mean burst duration; (D) Peak burst amplitude; (E) Mean burst amplitude

%, percentage; **s**, seconds; **MVE**, maximal voluntary exertion; **VL**, vastus lateralis; **BF**, biceps femoris; **BB**, biceps brachii; **TB**, triceps brachii

*Significantly different from VL; #Significantly different from BF; $Significantly different from BB; €Significantly different from TB

$p \leq 0.05$

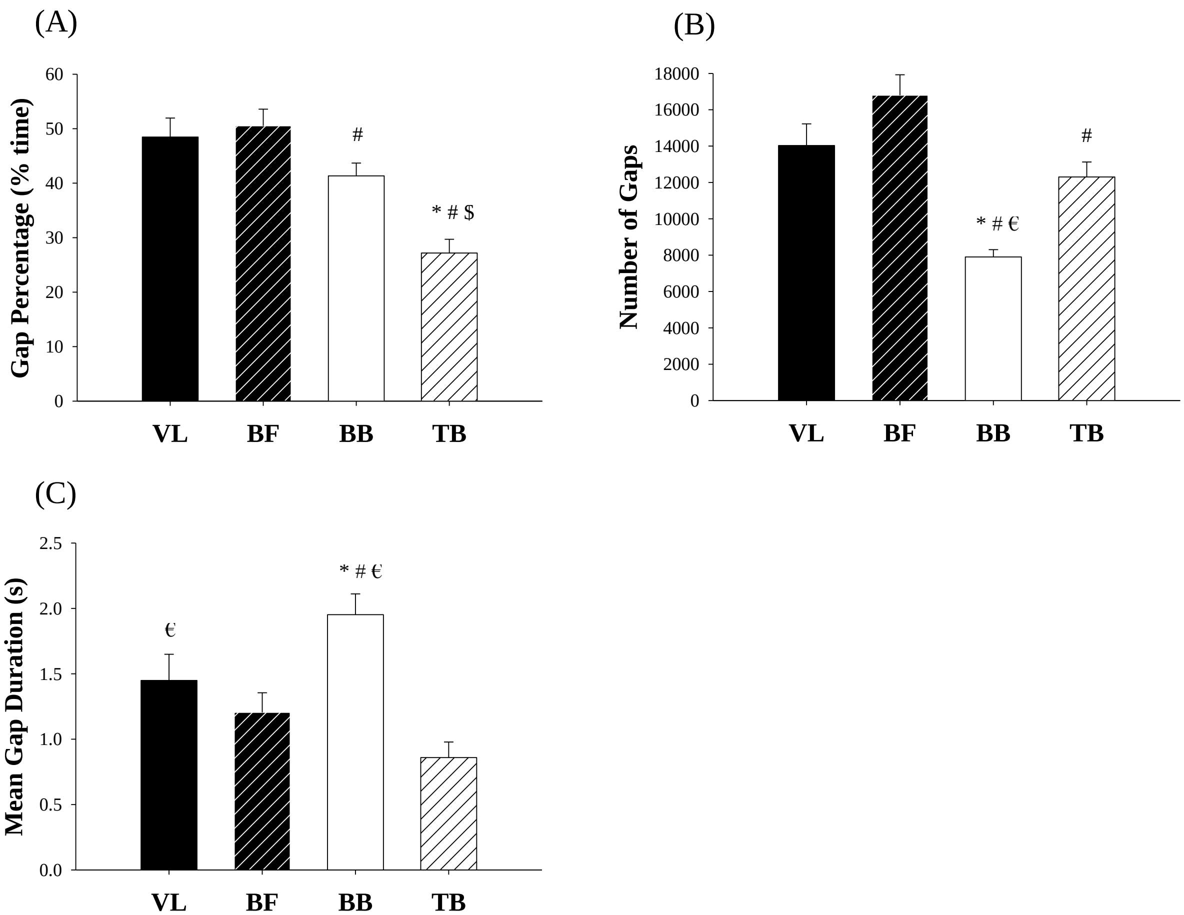

Figure 4.4. Gap Activity for the Vastus Lateralis, Biceps Femoris, Biceps Brachii, and Triceps Brachii

(A) Gap percentage; (B) Number of gaps; (C) Mean gap duration

%, percentage; **s**, seconds; **VL**, vastus lateralis; **BF**, biceps femoris; **BB**, biceps brachii; **TB**, triceps brachii

*Significantly different from VL; $^{\#}$Significantly different from BF; $^{\$}$Significantly different from BB; $^{€}$Significantly different from TB

$p \leq 0.05$

4.3.3 Relation between Mobility and Burst and Gap Characteristics

Number of steps was significantly related to all burst characteristics of the two thigh muscles (Figure 4.5). Pearson's correlations between the number of steps and the gap characteristics of the two thigh muscles were not significant (r = 0.01-0.22; p > 0.05).

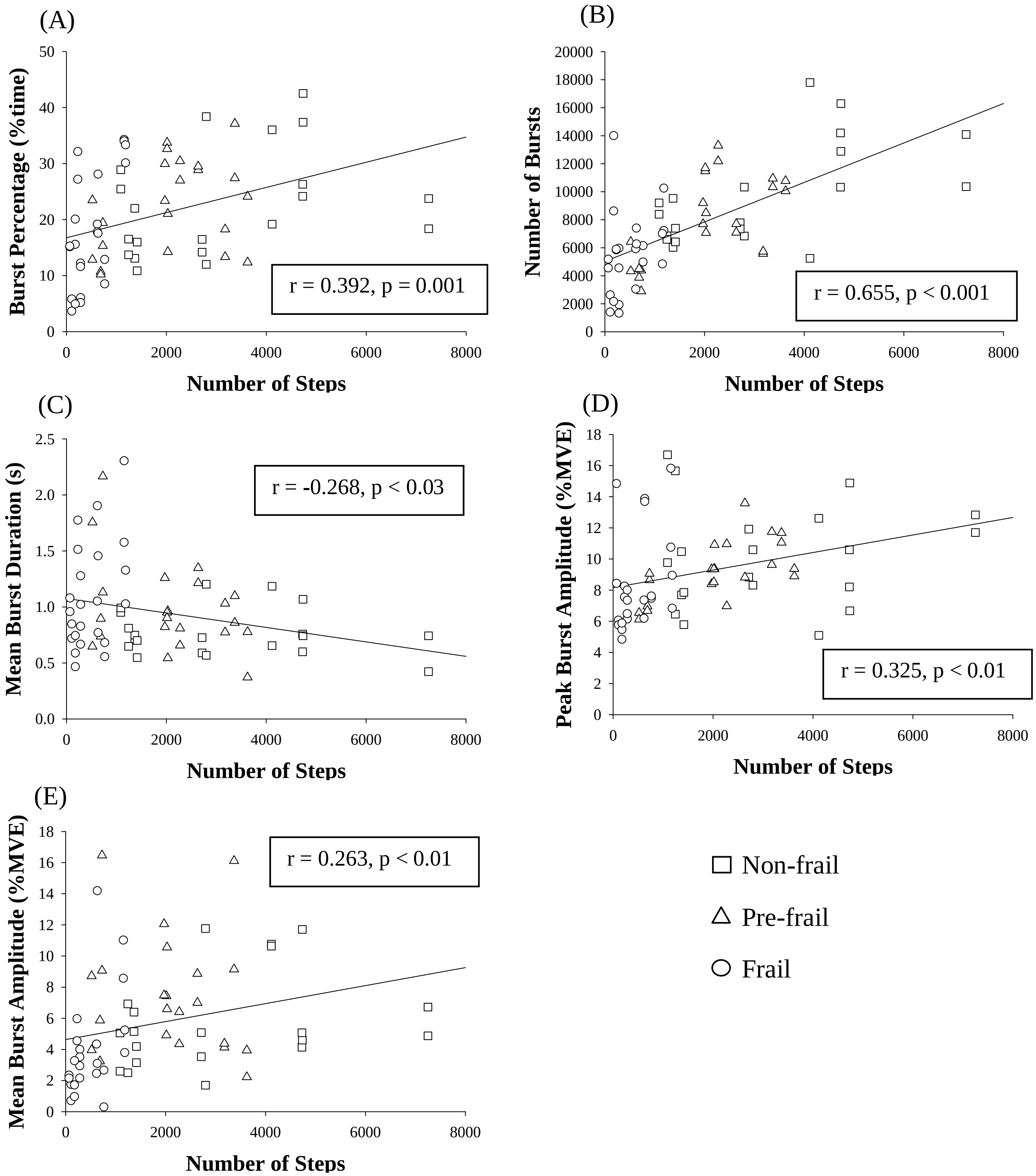

Figure 4.5. The Relationship Between Number of Steps and Burst Activity of the Two Thigh Muscles

(A) Bursts percentage; (B) Number of bursts; (C) Mean bursts duration; (D) Peak bursts amplitude; (E) Mean burst amplitude

r, pearson's correlation coefficient; **%**, percentage; s, seconds; **MVE**, maximal voluntary exertion

4.4 Discussion

Daily muscle activity and quiescence of the two arm (BB, TB) and two thigh (VL, BF) muscles, quantified by burst and gap activity, was compared between non-frail, pre-frail, and frail older women. To our knowledge this is the only study that has examined the association of EMG with frailty during daily life. The main outcome of this study was that the total duration that the muscles were active and quiescent was similar across all frailty groups. However, the characteristics of muscle activity and quiescence were different. Frail women activated their muscles fewer times but each activation was for longer duration compared with the non-frail women. In addition, muscle activity was greater in the arm muscles than the thigh muscles across all frailty groups and increased arm muscle activity was augmented in the TB. Thus, low-threshold EMG might provide a measure to dissociate stages of frailty and differences between upper and lower body muscle activity across all frailty stages.

The muscles of the older women in this study were active 26-30% of the time (burst percentage) which is equal to ~ 2.5 hours. Other studies found longer[30] or shorter duration[26,27] of daily muscle activity compared to our study. In these investigations, participants were younger,[26,27,30] different muscles were examined,[30] or a different methodological approach for data analysis was used.[26] Thus, differences in muscle activity beyond frailty status may arise from these experimental factors.

Mork and Westgaard[30] measured long-term EMG activity in the trapezius and low back muscles of sedentary young and middle aged women and found that the duration of muscle activity was 29-44% of the total recording time, which is similar to the total duration of muscle activity that we found for the arm muscles (30-39%). Kern et al.[27] found that VL and BB of women were active 12% and 23% of the recording time; however, these participants were young women which likely accounts for the shorter total duration of muscle activity compared with our study of older women. Howe and Rafferty[26] reported that the VL of women (mean age 64 years) was active 10% of the recording time which is less than the duration observed in these groups of non-frail, pre-frail, and frail women. These observed differences from previously published studies indicate that quantifying bursts and gaps enables dissociation of muscle activity between healthy young and older women as well as frail women. However, differences beyond frailty status likely arise from muscle activity being measured at varying thresholds of maximal EMG. Klein et al.[31] suggested that changing amplitude by 1% impacted the total duration of the daily muscle activity by 50-60%.

4.4.1 Effect of Frailty on Muscle Activity and Quiescence

Although the total duration of muscle activity and quiescence was similar across all frailty groups, independent characteristics of muscle activity and quiescence were different in the frail women compared with women in earlier stages of this syndrome (non-frail and pre-frail). The number of bursts observed in frail women was 28% fewer compared with the non-frail women, whereas there were 29% and 25% more EMG recorded gaps in frail women than non-frail and pre-frail women, respectively. This suggests that muscle activity was less in frail women relative to non-frail and pre-frail women. This study showed that muscle activity differs across the stages of frailty; however, it is not possible to determine whether frailty or changes in muscle activity comes first. Future longitudinal studies may address this question.

Frail women were older and 77-85% less mobile (steps completed during the day) than non-frail and pre-frail women. Mobility was highly correlated with the number of bursts across all frailty groups. Differences in chronological age and mobility likely account for the limited muscle activity observed in these frail older women. The number of steps completed in this study was much lower than those found in other studies even for the non-frail older adults.[32,33] However, we recorded steps only for nine hours compared with other studies that examine steps over a 24-hour period. In addition, physical activity participation measured by questionnaire in Greek older adults, was low compared with other European countries.[34] No studies have examined physical activity in Greek older adults using accelerometers but our data on non-frail older women suggest that physical activity is likely quite low. Actigraph accelerometer step counts have been shown to be accurate for walking speeds above 0.9 m/s but not for lower speeds,[33] thus the steps recorded in this study may have been underestimated especially for the frail older women.

Previous work in healthy mobile older adults has indicated that a reduction in the number of times that muscles were active is associated with an increase in the duration of each muscle burst.[19] Similarly, in our study burst number in frail women was less, but the duration of the bursts was longer. Specifically, mean burst duration of frail women was 26% longer than the non-frail women, while mean gap duration of frail women was 37% shorter compared with the pre-frail women. Fast velocity movements are more affected by aging than slow velocity movements,[14,35] which suggests that older frail women may move slower during the performance of activities of daily living than younger non-frail and pre-frail women. Differences in rate of movement might contribute to the greater mean duration of muscle activity in frail women compared with the other two groups. The amplitude of muscle activity each time muscles were active (mean burst amplitude) was 36% less in the frail women compared with the pre-frail women. Frail women's lower amplitude of muscle activity can also be related to their lower mobility level since they may have engaged in fewer tasks that would require the production of higher levels of force.

Muscle activity and quiescence discriminated later stage frailty, but only muscle activity characteristics discriminated early stage frailty (differences in pre-frail women compared with the non-frail women). Each burst in pre-frail women was approximately 30% longer with a 40% greater amplitude than the muscles of non-frail women. These two groups were of similar age, anthropometric and health characteristics, strength, and mobility. Factors such as impaired motor control and increased subjective fatigue, which are both outcomes of frailty, likely contribute to the differences in muscle activity.[13,23,36] Other physiological factors (e.g. muscle fiber-type proportion, motor unit firing rate, nerve conduction velocity, muscle fatigue) may also be related to differences between non-frail and pre-frail but studies have yet to examine the effect of frailty on these physiological characteristics. Future studies should extensively examine factors related to muscle activity difference across the stages of frailty and between sexes. It seems that low-threshold EMG may provide a measure of the onset of alterations in muscle activity that might assist in dissociating between early stages of this geriatric syndrome.

4.4.2 Differences Between Muscles on Muscle Activity and Quiescence

This study demonstrated that across all frailty groups thigh muscles were active 22% (~ 2 hours) and quiescent 50% (~ 4.5 hours) of the time. Compared to the thigh muscles the percentage of bursts were greater in the arm muscles. These results are consistent with a previous study in younger adults which reported that arm muscles are more active relative to thigh muscles.[27] The greater activity of the arm muscles compared with the thigh muscles (e.g. ~ 60% greater total duration of muscle activity) is likely because arm muscles relative to thigh muscles are not as strong[37] and they are needed extensively by older adults to execute activities of daily living (ADL).[38] Due to differences in strength and usage older women will need to engage arm muscles more than thigh muscles, which are needed for ambulation to support the body weight. Although arm muscles are not as strong as thigh muscles in both young and older adults, the age-related decline in strength is greater in the thigh muscles relative to arm muscles.[14,16,37,39,40] Lexell et al.[41] found that the loss of muscle mass in the VL begins approximately at 25 years of age with a 10% loss of muscle mass by 50 years of age. Thereafter the age-related decline accelerates and by 80 years of age, 40% of the muscle mass is lost.[42] Older women and especially frail women become less mobile as a result of their reduced thigh muscle mass and strength.[43,44]

Older women may spend much of their day seated or standing performing many household activities that use the arms. Thus, participation in daily life suggests that arm muscle movement is maintained relative to lower body ambulation. For example, upper body movement might increase frail older adults' use of their arms to help them rise from a chair relative to the lower body decrease. This can be detected as greater muscle activity and reduced muscle quiescence in the arm muscles compared with the thigh muscles. Future studies should examine how older women activate arm and thigh muscles to perform ADL (e.g. video analysis of ADL). A previous study[19] has shown that when the same task was performed there were age- and sex-related differences in muscle activity; however, the type of activities performed during the day may vary and contribute to differences in muscle activity across stages of frailty. Future laboratory studies need to examine whether differences in EMG activity between frailty stages is impacted by discrete tasks undertaken during the day in frail older adults and the degree of ambulatory mobility across these people. Through a combination of physical activity measures important information about frailty and function can be obtained but this was beyond the scope of this paper.

Muscle activity (except peak amplitude) and quiescence were similar in the two thigh muscles (VL, BF) across all three frailty groups. In contrast, differences in muscle activity and quiescence were found between the two arm muscles (BB, TB). Triceps brachii was active 39% of the time and quiescent 27% of the time; whereas BB was active 30% of the time and quiescent 41% of the time. Previous work in young adults indicated similarities in muscle activity between the lower limb muscles but not the upper limb muscles.[27] In addition, mean duration, mean amplitude, and peak amplitude of muscle activity were greater in the TB, whereas mean duration of muscle quiescence was greater in the BB. In contrast, the number of times that the muscles were active was similar between the two arm muscles and the number of times that the muscles were quiescent was greater in the TB. The observed differences between the two arm muscles in our study may be related to the greater strength of the BB compared with the TB and the greater usage of the TB for daily activities. A longitudinal study of older men described the rate of decline in muscle strength per year to be 1.6% and 1.8% for the TB and BB, respectively.[16] In addition, TB muscle mass[14] and its ability to activate[45] is better maintained with age than the BB and it may be relied on more to complete daily activities. This would result in greater muscle activity and less muscle quiescence, as observed. Alternatively, little is understood about fiber types between these muscles and thus differences in young adults as well as unique age-related changes within each muscle might contribute to the observed patterns of muscle activation between these arm muscles.[15]

4.5 Conclusions

Frailty did not affect the overall amount of muscle activity and quiescence, but the individual characteristics of each period of activity (bursts) and quiescence (gaps) differed. Thus, individual characterization might assist in classification between stages of frailty. Muscle activity discriminated both early and later stage frailty; however, muscle quiescence discriminated only later stage frailty. Mobility was associated with the differences observed in muscle activity across the stages of frailty. Even when mobility and strength, which are two known frailty indicators, were statistically similar between the non-frail and pre-frail women these groups differed for muscle activity. Therefore, muscle activity and quiescence differ across stages of frailty in older women and may add additional insight to the classification of frailty. Beyond the use of muscle activity and quiescence to dissociate frailty stages, they may also be used to indicate differences in muscle patterning. Arm muscle activity across all frailty groups was greater and quiescence was less compared with the thigh muscles, possibly because older adults use their upper limb muscles more than their lower limbs during the tasks of daily life.

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CHAPTER 5

The Effectiveness of Exercise Interventions for the Management of Frailty: A Systematic Review[a]

5.1 Introduction

Frailty is an increasingly recognized geriatric syndrome that has a tremendous impact on the older individual, their family, and society as a whole. The terms "frail" and "frailty" are often used in the literature without clear definition or criteria.[1] Frailty is a complex concept and the precise definition remains to be elucidated. However, there is broad support for the understanding that frailty is a state of vulnerability, caused by multi-system reduction, ranging in severity from mild to severe, that places the individual at increased risk of adverse health outcomes.[2,3] There is also a compelling need for effective interventions that manage frailty symptoms and as such, exercise may be the best medicine for this population.

Although numerous operational (clinical) definitions of frailty were proposed to help develop screening criteria, there is not yet a standardized and valid method of clinically screening for frailty.[4] The most commonly used definitions of frailty are the Frailty Phenotype,[5] the Frailty Index,[6] and the classification of Frailty and Vigorousness.[7] Fried et al.[5] proposed five frailty indicators: muscle weakness, subjective fatigue, reduced physical activity, slow gait speed, and weight loss. Rockwood and Mitnitski's[6] frailty index is based on a mathematical model of the accumulation of deficits where a deficit can be any symptom, sign, disease, disability, or laboratory abnormality. In Speechley and Tinetti's[7] classification older adults are classified as

[a] Article reprinted from submitted manuscript in the "Canadian Journal on Aging" with permission from the editor (Appendix G.4)

vigorous, transitional, or frail based on ten characteristics: age, gait/balance, walking activity for exercise, other physical activity for exercise, depression, use of sedatives, near vision status, upper and lower extremity strength, and lower extremity disability.

Frailty should be treated in order to prevent the human and economic burden associated with this syndrome. Mounting evidence suggests that exercise interventions can be used to maintain functional independence in older adults[8] and may potentially prevent, delay or reverse the frailty process.[9] The American College of Sports Medicine's (ACSM) position stand[10] on exercise for older adults recommends that exercise prescription for frail people is more beneficial than any other intervention and that the contradictions to exercise for this population are the same as those used with younger and healthier people. In addition, the most recently updated ACSM guidelines[11] recommend that resistance and/or balance training should precede the aerobic training for this population. However, recommendations on the appropriate design of the exercise protocol were not included.

There are several systematic reviews published on the benefits of exercise in older adults;[12-14] however, to our knowledge there are only two systematic reviews published specifically on the benefits of exercise in frail older adults.[15,16] Chin A Paw et al.[15] examined the effect of exercise on the functional ability of frail older adults. They included all studies that were published between 1995 and 2007, had identified their participants as frail either in the title or in the abstract, and focused only on functional outcomes. The authors concluded that exercise (resistance and multicomponent training) improved functional outcomes in this population. Daniels et al.[16] examined the effect of any type of intervention on disability in community-dwelling physically frail older adults. These investigators included studies that were published before 2007, used at least one of the frailty indicators as described by Ferrucci et al.[3] (mobility, strength, endurance, nutrition, physical inactivity, balance, motor processing) to identify their participants as frail, but focused solely on disability. The presence of only one frailty indicator does not necessarily warrant that participants were frail since frailty is thought to be caused by multi-system reduction.[2,3] These researchers suggested that multicomponent exercise training (consisting of endurance, flexibility, balance, and resistance training) reduced disability impact, especially in moderately frail people. Seven additional articles have been published since 2007 measuring the effect of exercise on broad range of outcome measures of frail older adults in addition to functional ability and disability. An updated systematic review of exercise interventions for frail older people, that comprehensively examines how frailty is assessed and does not focus only on one specific outcome measure, has yet to be completed. The purpose of this systematic review was to consider the use of the term “frailty” in relation to exercise interventions and to examine the effectiveness of current exercise interventions for the management of frailty.

5.2 Methods

5.2.1 Literature Search

A literature search using multiple electronic bibliographic databases was conducted. Medline (OVID; 1950-), Embase (OVID; 1974-), Psycinfo (Scholars Portal; 1806-), Cinahl (OVID & EBSCO; 1982-), Scopus (1823-), Ageline (AARP; 1978-), Eric (Proquest; 1966-), and SportDiscus (EBSCO; 1800-) were searched up to February 1, 2009. Reference lists of all relevant articles were cross-referenced by hand searching in order to identify additional articles. The primary search terms that were used for searching the electronic databases were frail and all reasonable expressions of exercise. The search strategy that was used for Medline is included in Appendix D.

5.2.2 Inclusion/Exclusion Criteria

Studies met the following inclusion criteria; 1) acknowledged as a randomized-controlled trial, 2) full-text published in either English or French, 3) study participants were identified as ‘frail’ in either the title, abstract and/or text, 4) exercise was acknowledged as an independent component of the intervention. Exercise was defined as a form of physical activity that was structured and repetitive over an extended period of time, with the intention of improving fitness, performance or health.[17] Although frailty usually interacts with other chronic conditions, the purpose of this systematic review was to focus exclusively on frailty; therefore those studies that targeted specific chronic disease conditions were excluded.

5.2.3 Data Collection and Analysis

The database search results were uploaded into a web-based system[18] which was used to manage the screening process. Duplicate citations were removed. To determine which studies would be included two members of the review team independently screened the title and abstracts of the articles that were extracted from the literature search. The full-text was retrieved electronically for studies that met reviewers' agreement based on the inclusion/exclusion criteria. For each article that satisfied these criteria two reviewers independently extracted the following data; country that the study was conducted, number of participants in the intervention and control groups, age of participants at inclusion, sex of participants, living arrangements, inclusion criteria used to recruit participants, frailty definition that was used, characteristics of the exercise intervention (frequency, intensity, duration, and type), and outcome measures. Any disagreement on papers and data extracted between the two reviewers was resolved by a third reviewer.

The methodological quality of the included studies was evaluated by two reviewers using the Jadad Methodological Quality Criteria scale.[19] The double blinding criterion for this scale was modified due to the inability to blind allocation of study participants to an exercise intervention. A study could receive a Jadad score of zero to five. Differences in rating between the two reviewers were resolved by a third reviewer. The questions used were:

- Was the method of randomization described in the paper? (2 points)
- Were the outcome assessors blinded to treatment allocation? (2 points)
- Was there a description of withdrawals and dropouts? (1 point)

Although we included all published outcome measures, for reporting we grouped these measures into three areas:

Physical and psychosocial determinants included body composition, nutrition status, biochemical status, cardiorespiratory function, muscle function, flexibility, physical activity participation, neurological and cognitive function, psychosocial state.

Functional ability included mobility, balance, and functional performance test batteries.

Adverse health consequences included ADL (Activities of Daily Living) disability, quality of life, falls, and utilization of resources

Due to variability in participant and intervention characteristics, assessment tools used to diagnose frailty, and outcome measures used across studies, a meta-analysis could not be satisfactorily performed. Meta-analysis should only be considered when a group of studies have sufficient homogeneity between participants, interventions and outcomes to provide a meaningful summary. In accordance with the Cochrane library if there is substantial clinical diversity a qualitative approach combining studies is appropriate. Previous systematic reviews on exercise and frailty[15,16] did not conduct a meta-analysis for similar reasons. Subgroup analysis was done to examine factors that may explain the variability of these results. The outcomes were stratified based on; the participants' characteristics (mean age, sex, and living arrangements), if a current frailty definition was used in the study, the intervention characteristics (frequency, intensity, duration, and type), and the methodological quality. We report the percentage of those outcome measures that significantly improved due to the exercise interventions.

5.3 Results

5.3.1 Description of Studies

The preliminary search yielded 2247 citations. After an initial screening of all titles and abstracts 303 articles remained from which full text were obtained. Of these articles 74 met the inclusion/exclusion criteria.[20-93] The inter-rater reliability using Kappa score was 0.73 during screening of titles and abstracts and 0.80 during screening of full text articles. One article was identified by hand searching the reference lists of all relevant articles and reviews.[94] Articles using the same participants and intervention were grouped as a single study although multiple subsets of the data were published independently. Therefore, 75 published articles described 47 studies (Figure 5.1). Eleven studies published multiple articles with various outcomes.[20-57,94] For the purpose of this review we state the number of studies, while the citation indicates all published articles associated with those studies. All relevant articles were published after 1993 and the majority (85%) were published after 2000.[20-58,60-62,64,65,68-76,78-90,92,94] Nineteen of the selected studies[28-38,47-54,58-71] were from the USA, 18[20-27,39-46,55-57,72-83] from European countries, five[84-88] from Japan, three[89-91] from New Zealand and Australia, and two[92,93] from Canada. The number of participants in the articles varied from 13[59] to 551[89] and a total of 4915 participants were included in this systematic review.

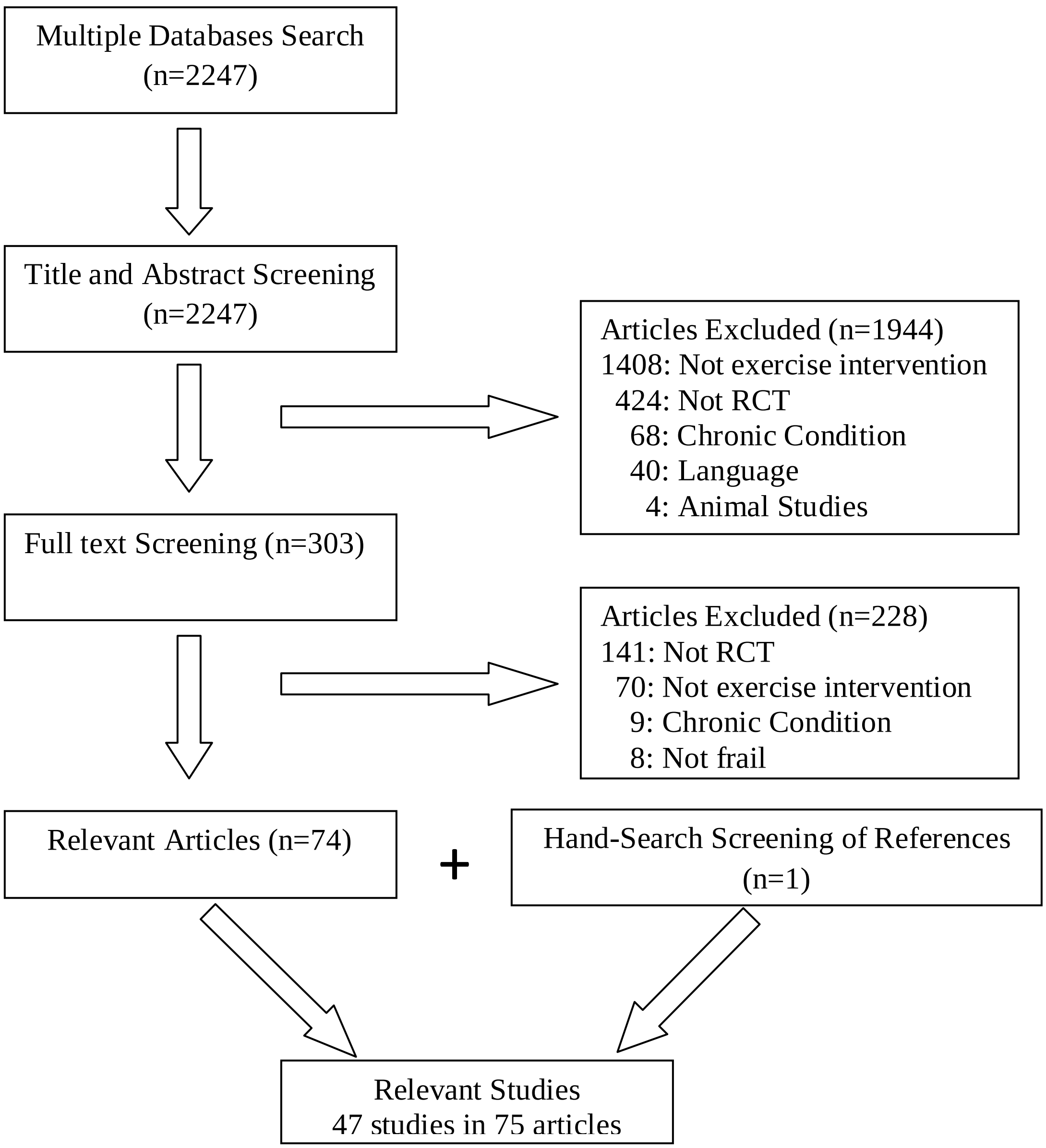

Figure 5.1. Flow Chart of Article Screening
RCT, Randomized Controlled Trial

5.3.2 **Participants Characteristics**

Participants of all studies were older than 60 years. The mean age ranged from 71[60] to 90 years[81] and the mean age of the participants in all the included studies was 81.5 years. Nineteen studies[43-49,66-69,77-82,85,87,88,91-93] targeted those living in long-term care facilities (LTC) (table 5.1), 16[20-40,58-64,72,73,75,84] focused on community-dwelling older adults (table 5.2), one[86] included both community and LTC, four[50-54,65,76,89] were conducted in retirement homes, one[41,42] included both community and retirement homes (table 5.3), and six[55-57,70,71,74,83,90,94] involved hospital care (table 5.4). Most (74.5%) of the included participants were women. In six studies[45,46,55-57,61,74,75,88,94] participants were only women and in two studies[59,71] only men, three studies[80,87,91] did not specify the sex of the participants, and all remaining studies[20-44,47-54,58,60,62-70,72,73,76-79,81-86,90,92,93] included both sexes (women were the majority in most of them). There were too few studies, that measured adverse health consequences, where men were more abundant than women to suggest any sex differences in the effect of exercise on this outcome (table 5.5).[63]

Table 5.1. Description of Studies That Were Done in Long Term Care

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
194 (71) 81	>60, Living in LTC and experiencing ADL disability [d]	Multicomponent one-on-one training (physical therapy), 16 weeks, 3/week, 30-45min/session	Cognition (MMSE), Depression (Geriatric Depression Scale); Test Batteries (physical disability index); ADL Disability (Katz ADL); QOL (sickness impact profile); Utilization of resources (health care cost)	5	67
191 (73) 85	>65, Living in LTC and experiencing ADL disability [d]	High intensity functional multicomponent training (resistance, balance, walking), 12 weeks, 2-3/week, 45min/session,8–12 rep based on 1RM	**Muscle Function (lower strength); Walking Speed (2.4 meters test); Balance (BBS);** Falls (incident rate)	5	43, 44
190 (84) 88	Nursing home residents, incontinence [d]	Functional multicomponent training (aerobic, resistance), 32 weeks, 5/week, 75% of maximum workload	Biochemical status (Lymphocyte subpopulations); **Cardio (exercise HR); Muscle Function (upper strength); PA (motion sensors and staff observations); Mobility Endurance (walked or wheeled distance)**	5	68
97 (84) 84	>65, physically restrained nursing home residents, extremely impaired both cognitively and physically [d]	Mutlicomponent training (aerobic, resistance, mobility, safety practice), 9 weeks, 3/week, 10% increase/week	**Psychosocial State (safety score); Muscle Function (upper strength and endurance); Flexibility (rowing ROM);** Mobility Endurance (walk time, **wheel time**); Chair Rises (30 sec)	3	66

(Table 5.1 continued pg.107)

Table 5.1. (Continued)

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
30 (50) 81	Living in LTC, mild cognitive impairment [d]	Multicomponent training (aerobic, resistance, balance, flexibility), 4 weeks	**Psychosocial State (behavioral problems and use of antipsychotic and hypnotic medications)**	1	79
20 (75) 88	>65, Living in LTC [d]	Multicomponent training (resistance, flexibility), 48 weeks, 3/week, 60min/session, 1X5-2X10 rep	**Cognition (MMSE); TUG; Balance (BBS); Test Batteries (PPT)**	5	69
71 82	Living in LTC [d]	Multicompont training (aerobic, resistance, balance, flexibility, coordination), 48 weeks, 2/week, 10-60min	**Psychosocial State (class satisfaction); PA (daily activity level); Chair Rises**	4	91
68 (87) 80	Living in LTC [d]	Multicomponent training (resistance, balance, flexibility, walking), 16 weeks, 3/week, 45min/session	**Muscle Function (lower and upper strength); Flexibility (sit and reach, shoulder flexion);** Walking Speed (7 meters test); **TUG**; Stair Climb (3 steps); **Balance (BBS); ADL disability (FIM)**	5	93
100 (63) 87	>75, Living in LTC [d]	High-intensity progressive resistance training of the hip and knee extensors, 10 weeks, 3/week, 45min/session, 3X8 at 80%1RM	Body composition (weight, **muscle mass**, muscle fiber distribution); **Nutrition (energy intake)**; **Biochemical (**muscle damage **and regeneration,** central nuclei**, IGF-1); Muscle Function (lower strength); PA (activity monitor); Walking Speed (6.1 meters test); Stair Climb (4 steps)**	3	47-49

(Table 5.1 continued pg.108)

Table 5.1. (Continued)

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
22 82	>70, Living in LTC [d]	Progressive resistance training, 10 weeks, 3/week, 3X8 rep at 40% and 80%1RM	**Muscle Function (KE strength and endurance); Mobility Endurance (6-minute walking test); Chair Rises (3 times); Stair Climb (4 steps); ADL disability (health assessment questionnaire disability index subscale)**	5	80
41 (80) 81	Living in LTC [d]	Resistance training with music, 28 weeks, 2/week, 45min/session	Cognition (MMSE), **Depression (Geriatric Depression Scale); Muscle Function (grip strength)**; Flexibility (KE and KF, **Spinal flexion ROM**); **Chair Rises**; Balance (postural sway); **ADL Disability (Barthel Index)**	3	77
25 (76) 83	Living in LTC [d]	Progressive lower body resistance training (aimed at improving muscle power), 10 weeks, 3/week, 20-60min/session	**Muscle Function (KE strength and power); Walking Speed (6 meters test); Chair Rises (30 sec); TUG**	3	92
21 (90) 90	Living in LTC [d]	Resistance training of knee extensors and flexors, 12 weeks, 3/week, 45min/session, 3X8 rep at 50-80%1RM	Biochemical status (inflammatory markers); **Muscle Function (KE and KF strength)**	2	81

(Table 5.1 continued pg.109)

Table 5.1. (Continued)

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
278 (68) 85	frail and prefrail (Fried's frailty phenotype) [a]	Functional Walking, Balance, 20 weeks, 2/week, 90min/session	**Test Batteries (POMA, physical performance score based on 4 tests); ALD Disability (GARS)**; Falls (incident rate)	5	78
27 (100) 82	>70, Living in LTC [d]	Visual feedback-based balance training, 4 weeks, 3/week, 20-30min/session	**PA (interview); Balance (postural sway, weights shifting, BBS); Falls (incident rate, fear of falling)**	3	45,46
32 (78) 83	Living in LTC [d]	Treadmill walking training, 24 weeks, 1-3/week, 50-70% of the maximum speed	**Neurological (auditory stimulus reaction time);** Walking Speed (10 meters test); **Balance (one leg stance, functional reach);** Falls (incident rate, time to first fall)	2	85
30 77	>65, inactivity, ADL disability [c]	Water training (resistance, flexibility, activities of daily living (ADL) exercises, relaxation), 24 weeks, 1-2/week, 60min/session, intensity based on Borg's RPE scale	**ADL disability (FIM); QOL (SF-36)**	5	87
24 (63) 78	Living in LTC and experiencing ADL disability [d]	Whole Body Vibration training, 6 weeks, 3/week	Muscle Function (lower and upper strength); Flexibility (back scratch, chair sit-and-reach); Chair Rises (30 sec); **TUG; Test Batteries (POMA)**	5	82

(Table 5.1 continued pg.110)

Table 5.1. (Continued)

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
145 (100) 86	Living in LTC [d]	Exercise therapy using the Takizawa Program, 12 weeks, 3/week	**Flexibility (shoulder, knee, ankle dorsiflex ROM);** ADL disability (FIM)	5	88

a Validated operational definition of frailty

c At least one frailty indicator in the inclusion criteria

d No frailty indicators on the inclusion criteria

e Significant between group differences are shown in **bold**

1RM, one repetition maximum; **ADL,** activities of daily living; **BBS,** Berg Balance Scale; **FIM,** Functional Independence Measure**;** **GARS,** Groningen Activity Restriction Scale; **HR,** Heart rate; **IGF-I,** Insulin-like growth factor I; **KE,** knee extension; **KF,** knee flexion; **LTC,** long term care; **MMSE,** mini-mental status exam; **PA,** physical activity; **POMA,** Tinetti performance oriented mobility assessment; **PPT,** Physical performance test; **QOL,** Quality of life; **rep,** repetitions; **ROM,** Range of motion; **RPE,** rating of perceived exertion; **SF-36,** Medical Outcomes Survey Short-Form 36; **TUG,** timed up-and-go test

Table 5.2. Description of Studies That Included Community-Dwelling Older Adults

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
188 (80) 83	moderate and severe physical frail (walking test and chair stand test), >75 [b]	Multicomponent training (resistance, balance, flexibility), 24 weeks, 3/week, up to 60min/session, 2X10 rep at three levels of difficulty	**Walking Speed (3 meters test); Chair Rises (3 times); Test Batteries (POMA, PPT); ADL Disability (8 ADL scale, IADL scale)**; **Falls (fear of falling)**; Utilization of resources (admission and days spent in nursing home)	5	32-35
161 (71) 79	frail (reduced physical activity and weight loss) [b]	Supervised group functional multicomponent training (aerobic, resistance, flexibility, speed, coordination, skills training), 17 weeks, 2/week, 45min/session, intensity 6-8 on a 10-point perceived exertion scale	Body composition (**weight, muscle mass**, fat mass, bone mass); Nutrition (**energy and carbohydrate intake**, fat and protein intake, haematological indicators, sensory performance and appetite); **Biochemical (cellular immune response)**; Neurological (visual stimulus reaction time, coordination); Psychosocial State (social involvement); **Groningen fitness test for the elderly (strength, flexibility, balance, block transfer, reaction time); Test Batteries (Functional performance based on six performance tests);** ADL disability (self-reported ability to perform 16 ADL); QOL (Dutch scale of subjective wellbeing for older persons, self-rated health)	4	20-27

(Table 5.2 continued pg.112)

Table 5.2. (Continued)

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
155 (79) 77	frail (SPPB and the indication of difficulty with ADL), >70 [b]	Class-based multicomponent training (functional aerobic, resistance, flexibility), 72 weeks, 3/week, 75min/session	Only exercise compliance	5	58
115 (52) 83	mild to moderate physical frail (PPT, difficulty with ADL, and reduced peak aerobic power), >78 [b]	Multicomponent (physical therapy, aerobic, resistance), 36 weeks, 3/week, 20-60min/session, 3X8-12 rep at 85-100%1RM, 15 min at 65-70%VO_2max and 3-5 min 85-90%VO_2max	Body composition (weight, **muscle mass**, fat mass, bone mass); Nutrition (energy intake); Cardio (**VO_2max, cardiac output, exercise HR and peak BP**, resting HR and BP, **left ventricular stroke work); Muscle Function (lower and upper strength); Balance (one leg stance, BBS); Test Batteries (PPT, Functional Status Questionnaire);** ADL Disability (The Older American Resources and Services Instrument); **QOL (SF-36)**	5	28-31
96 (60) 83	frail (reduced physical activity and weight loss), >75, receiving home service. age under 75, body mass index <30 kg/m^2 [b]	Multicomponent training (aerobic, resistance, Qigong), 12 weeks, 2/week, 60min/session, 60-80% intensity	Body composition (weight, muscle mass); Nutrition (energy intake); Psychosocial State (health belief model); **Muscle Function (lower and upper strength);** Walking Speed (10 meters test); **Chair Rises (30 sec)**; TUG; **Stair Climb (30 sec)**; Balance (one leg and tandem stance, **modified figure 8**); ADL Disability (FIM, IAM)	3	72

(Table 5.2 continued pg.113)

Table 5.2. (Continued)

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
84 (57) 83	mild to moderate physical frail (PPT), >78, sedentary, living independently but with difficulty [b]	Low-intensity supervised multicomponent training (resistance, balance, flexibility, body handling skills, speed of reaction, coordination), 12 weeks, 3/week, three levels of difficulty for each exercise	Neurological (visual stimulus reaction time, light touch and pressure sensation and proprioception, **coordination**); **Muscle Function (lower and upper strength); Flexibility (shoulder, hip, knee, trunk ROM);** Walking Speed; **Balance (one leg stance, obstacle course, BBS); Test Batteries (PPT)**	2	62
77 (81) 81	physical frail (at least one fall during the last year and used some kind of walking aid either indoors or outdoors), >75 [b]	Functional multicomponent training (resistance, balance), 12 weeks, 2/week, 40min/session	**Psychosocial State (satisfaction); PA (interview, frequency and duration of outdoor walks); Walking Speed (3 meters test); QOL (SF-36)**	5	73

(Table 5.2 continued pg.114)

Table 5.2. (Continued)

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
53 (100) 82	frail (reduced physical activity and unable to get outdoors without walking aids or help from another person and/or subjective functional ability), >75, receiving practical and/or personal public home care [b]	Home-based multicomponent training (aerobic, resistance, flexibility, dynamic balance), 20 weeks, 3/week, 26min/session	**Psychosocial State (Mobility-tiredness scale)**; Muscle Function (lower power and **upper strength**); **Walking Speed (10 meters test); Chair Rises (5 times)**; Balance (stance); **Test Batteries (PPT);** QOL (EQ-5D questionnaire, self-rated health status)	3	75
424 (69) 77	70–89, inactivity, risk for major mobility disability as indicated by a summary score of ≤9 on the SPPB (balance, mobility, strength) [c]	Multicomponent training (aerobic, resistance, balance, flexibility, walking), 48 weeks, 1-3/week, 60min/session, intensity based on Borg's RPE scale	**Psychosocial State (Self-efficacy for the 400-m walk, satisfaction with physical function); PA (CHAMPS Questionnaire)**	5	64

(Table 5.2 continued pg.115)

Table 5.2. (Continued)

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
13 (0) 75	>70, at risk for fall (history of fall past year, muscle weakness, measurable gait or balance impairment) [c]	Multicomponent training (resistance, balance, walking), 12 weeks, 3/week, 60min/session	**Biochemical status (Immune)**	3	59
46 (59) 81	referred by their general practitioner and patients who could not leave their home by themselves [d]	Multicomponent and comprehensive training (aerobic, resistance, balance, flexibility, rhythm, reaction), 12 weeks, 2/week, 60min/session	Body composition (muscle and fat mass), **Cardio ($V0_2$max); Muscle Function (upper strength); Walking Speed (10 meters test); Balance (BBS); QOL (SF-36)**	2	39,40
100 (50) 78	frail (inability to descend stairs step over step without holding the railing) [b]	Home-based resistance training, 10 weeks, 3/week	**Muscle Function (lower strength); Walking Speed (10 meters test)**; Mobility endurance (6-minute walk test); **Chair Rises (lowest height someone stands)**; Balance (postural sway, functional reach); **Test Batteries (mobility skills protocol);** QOL (SF-36); **Falls (fear of falling)**	5	63
31 (35) 71	moderate frail (PPT) [b]	Resistance training, 24 weeks, 3/week, 60min/session, 3X8 rep based on 1RM	Body composition (muscle mass, muscle fiber distribution); Biochemical (IGF-I); **Muscle Function (KE strength)**	2	60

(Table 5.2 continued pg.116)

Table 5.2. (Continued)

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
21 (100) 78	>70, SPPB score 4-10 (balance, mobility, strength)[c]	Progressive resistance training (mobility task-specific and one component at the fastest possible velocity), 12 weeks, 3/week, 30min/session, 3 sets	**Muscle Function (lower power); Walking Speed (2.4 meters test); Chair Rises (5 times); Balance (one leg stance); Test Batteries (SPPB)**	4	61
17 (71) 82	mild to moderate physical frail (PPT and difficulty with ADL) [b]	Resistance training, 24 weeks, 3/week, initially 1–2X6–8 rep at 65–75%1RM and progressed to 3X8–12 rep at 85–100%1RM	Body composition (weight, **muscle mass**); **Biochemical status (muscle protein synthesis, TNF-a, LPL protein content); Muscle Function (lower and upper strength)**	2	36-38
21 (48) 80	>65, Using the day care facility 2 or more times per week [d]	Horse riding simulator training, 12 weeks, 2/week, 10-30min/session, speed of the simulator based on the physical activity of participants	**Walking Speed (5 meters test)**; TUG; **Balance (stance, spinal alignment, functional reach)**	2	84

b Non-validated operational definition of frailty

c At least one frailty indicator in the inclusion criteria

d No frailty indicators on the inclusion criteria

e Significant between group differences are shown in **bold**

(Table 5.2 continued pg.117)

1RM, one repetition maximum; **ADL,** activities of daily living; **BBS,** Berg Balance Scale; **BP,** Blood pressure; **FIM,** Functional Independence Measure**; HR,** Heart rate; **IADL,** Instrumental activities of daily living; **IAM,** Instrumental activity measure; **IGF-I,** Insulin-like growth factor I; **KE,** knee extension; **LPL,** Lipoprotein lipase; **PA,** physical activity; **POMA,** Tinetti performance oriented mobility assessment; **PPT,** Physical performance test; **QOL,** Quality of life; **rep,** repetitions; **ROM,** Range of motion; **RPE,** rating of perceived exertion; **SF-36,** Medical Outcomes Survey Short-Form 36; **SPPB,** Short physical performance battery; **TNF-a,** Tumor necrosis factor-alpha; **TUG,** timed up-and-go test; **VO_2max,** maximal oxygen uptake

Table 5.3. Description of Studies That Were Done in Retirement homes and in Mixed Settings

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
311 (94) 81	Transitionally frail (Speechley and Tinetti's Classification of Frailty and Vigorousness), living in retirement home, >70, at least one fall within the past year [a]	Tai Chi, 48 weeks, 2/week, 60 min and progress to 90 min/session	Body composition (weight, body mass index); **Cardio (resting HR and BP); Walking Speed; Chair Rises (3 times)**; Balance (one leg stance, **functional reach**, picking up an object from the floor, 360 turn, **postural control**); QOL (Sickness Impact Profile, self-rated health); Falls (incident rate, **fear of falling)**	5	50-54
57 (88) 84	Frail (age, comorbidity, polypharmacy, and prolonged stay in retirement home) [b]	Multicomponent training (resistance, balance, flexibility), 36 weeks, 3/week, 60min/session,	Body composition (body mass index, muscle mass); Nutrition (haematological indicators, resting energy expenditure); Muscle Function (KE power); Walking Speed (6 meters test); **Chair Rises (5 times)**; Stair Climb (3 steps)	3	76
551 (86) 80	Living in retirement home [d]	Functional multicomponent training (aerobic, resistance, balance, flexibility, coordination), 48 weeks, 2/week, 60min/session	**Neurologic (visual stimulus reaction time)**; Muscle Function (KE strength); **Mobility endurance (6-minute walk test)**; Balance (postural sway, maximal balance range and coordinated stability tests); **Falls (incident rate)**	3	89

(Table 5.3 continued pg.119)

Table 5.3. (Continued)

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
161 (86) 82	>65, living in retirement home and experiencing ADL disability [d]	Task-specific resistance training (training in bed- and chair-rise subtasks), 12 weeks, 3/week, 60min/session	Muscle Function (lower, upper, **trunk strength**); **Flexibility (trunk, arm, leg ROM); Chair Rises (Bed- and Chair- rise task); Balance (trunk)**	3	65
49 (92) 79	Living at community or retirement home, KE muscle weakness[c]	Resistance training, 10 weeks, 3/week, 60min/session, 3X4 rep	**Muscle Function (isometric knee strength); Walking Speed (20 meters test); TUG**; Stair Climb (box-stepping); Balance (parallel, semi-tandem, and tandem stance); ALD Disability (GARS)	4	41,42
34 (85) 81	Living at community or LTC [d]	Walking exercises, Balance training, 12 weeks, 2-3/week, 40min/session	**TUG**; Stair Climb (5 steps); Balance (**one leg stance, functional reach**, Manual Perturbation Test, **Functional Balance Scale**); **Test Batteries (POMA)**	3	86

a Validated operational definition of frailty

b Non-validated operational definition of frailty

c At least one frailty indicator in the inclusion criteria

d No frailty indicators on the inclusion criteria

e Significant between group differences are shown in **bold**

ADL, activities of daily living; **BP,** blood pressure; **GARS,** Groningen Activity Restriction Scale; **HR,** heart rate; **KE,** knee extension; **LTC,** long term care; **POMA,** Tinetti performance oriented mobility assessment; **QOL,** quality of life; **rep,** repetitions; **ROM,** range of motion; **TUG,** timed up-and-go test

Table 5.4. Description of Studies That Included Hospitalized Older Adults

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
76 (72) 85	>70, acutely ill patients, acutely bedridden or with reduced mobility [c]	Multicomponent training (intensive physiotherapy), 48 weeks, 5/week, 30min/session	Body composition (weight, body mass index, fat mass, arm and calf circumference); **Nutrition (energy and protein intake, haematological indicators); Muscle Function (grip strength); ADL Disability (Katz ADL)**	2	83
68 (100) 83	>75, admitted to a geriatric ward of primary-care health center hospital for an acute illness, difficulties in mobility and balance, and symptoms such as dizziness, reported falls or difficulty to walk independently [c]	Multicomponent training (resistance, functional exercises, relaxation), 10 weeks, 2/week, 90min/session, 2X8-10 rep	**Depression (Zung self-rating Depression Scale; Muscle Function (lower isometric strength); Walking Speed (10 meters test); Balance (BBS);** ADL Disability (Joensuu classification); Falls (incident rate); Utilization of resources (health care, social welfare, and falls cost)	3	55-57 94

(Table 5.4 continued pg.121)

Table 5.4. (Continued)

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
57 (100) 82	>75, Older adults admitted to a hospital due to a fall or with a history of injurious fall that required medical treatment [d]	Functional multicomponent training (resistance, balance), 12 weeks, 3/week, 70-90% of maximum workload	Depression (Geriatric Depression Scale); Psychosocial State (emotional status); Muscle Function (**lower** and upper strength); **PA (Questionnaire); Walking Speed (15 meters test); Chair Rises (3 times); TUG; Stair Climb (13 steps); Balance (stance, functional reach); Test Batteries (POMA)**; ADL Disability (Barthel Index and the Lawton Index of IADL); Falls (incident rate, **fear of falling**, **walking steadiness, emotional instability and behavioral changes following a fall)**	5	74
243 (53) 79	frail (Winograd's frailty scale), >65 [a]	Home-based resistance training, 10 weeks, 3/week, 3X8 rep at 60-80%1RM	**Psychosocial State (degree of fatigue)**; Muscle Function (KE strength); Walking Speed (4 meters test); TUG; Balance (BBS); ADL Disability (Barthel Index and Adelaide Activities Profile); QOL (SF-36); Falls (incident rate, time to first fall, fear of falling)	5	90

(Table 5.4 continued pg.122)

Table 5.4. (Continued)

N (%F) Mean Age	Inclusion Criteria	Intervention Characteristics	Outcome measures [e]	Quality	Reference
71 (0) 78	>65, hypogonadal recuperative care patients, recent functional decline [c]	Progressive resistance training, 12 weeks, 3/week, 3X8 rep at 20% and 80%1RM	Body composition (muscle mass); **Muscle Function (lower and upper strength);** Test Batteries (aggregate functional performance test)	5	71
29 (17) 79	>65, recent illness-induced functional decline [c]	Progressive resistance training, 12 weeks, 3X8 rep at 20% and 80%1RM	Body composition (**weight**, muscle mass, **fat mass**); Nutrition (energy intake); Muscle Function (lower and **upper strength**); Test Batteries (aggregate functional performance test)	5	70

a Validated operational definition of frailty

c At least one frailty indicator in the inclusion criteria

d No frailty indicators on the inclusion criteria

e Significant between group differences are shown in **bold**

1RM, one repetition maximum; **ADL,** activities of daily living; **BBS,** Berg Balance Scale; **IADL,** Instrumental activities of daily living; **KE,** knee extension; **PA,** physical activity; **POMA,** Tinetti performance oriented mobility assessment; **QOL,** Quality of life; **rep,** repetitions; **SF-36,** Medical Outcomes Survey Short-Form 36; **TUG,** timed up-and-go test

Table 5.5. **Percentage of Outcome Measures That Improved due to the Exercise Interventions**

	Physical & Psychosocial Determinants	Functional Ability	Adverse Health Consequences	Reference
All studies	60%	71%	39%	20-94
Age				
71-79 years	43%	48%	23%	20-27,41,42,58-61,63,64,70,71,82,87,90
80-90 years	66%	76%	44%	28-40,43-57,62,65-69,72-81,83-86,88,89,91-94
Sex				
Women>Men	61%	73%	39%	20-58,61,62,64-69,72-78,80-83,85-94
Men>Women	53%	54%	-------	59,60,63,70,71,79,84
Living Arrangement				
Long Term Care	76%	78%	50%	43-49,66-69,77-82,85,87,88,91-93
Community	57%	77%	44%	20-40,58-64,72,73,75,84
Retirement Home	41%	53%	40%	50-54,65,76,89
Hospital Care	50%	64%	25%	55-57,70,71,74,83,90,94

(Table 5.5 continued pg.124)

Table 5.5. (Continued)

	Physical & Psychosocial Determinants	Functional Ability	Adverse Health Consequences	Reference
Include Operational Definition				
Yes	50%	64%	30%	20-38,50-54,58,60-63,72,73,75,76,78,90
No	68%	75%	48%	39-49,55-57,59,61,64-71,74,77,79-89,91-94
Include Moderate Frail				
Yes	62%	82%	50%	28-38,50-54,60,62,78
No	60%	68%	36%	20-27,39-49,55-59,61,63-77,79-94
Type of Intervention				
Multicomponent Training	58%	75%	40%	20-35,39,40,43,44,55-59,62,64,66-69,72-76,79,83,89,91,93,94
Resistance Training	67%	61%	27%	36-38,41,42,47-49,60,61,63,65,70,71,77,80,81,90,92
Frequency of Intervention				
2/week	51%	67%	35%	20-27,39,40,50-57,72,73,77,78,84,89,91,94
3/week	62%	72%	39%	28-38,41,42,45-49,58-63,65-67,69,71,74-76,80-82,88,90,92,93

(Table 5.5 continued pg.125)

Table 5.5. (Continued)

	Physical & Psychosocial Determinants	Functional Ability	Adverse Health Consequences	Reference
Duration of Intervention				
1-4 months	61%	70%	30%	20-27,39-49,55-57,59,61-63,65-67,70-74,79-82,84,86,88,90,92-94
5-18 months	59%	74%	52%	28-38,50-54,58,60,64,68,69,75-78,83,85,87,89,91
Duration per Session of Intervention				
30-45 minutes	60%	78%	43%	20-27,43-49,61,67,73,75,77,81,83,84,86,93
60-90 minutes	49%	60%	38%	39-42,50-60,64,65,69,72,76,78,87,89,94
Methodological quality				
0-4 Jadad score	60%	69%	33%	20-27,36-42,45-49,55-57,59-62,65,66,72,75-77,79,81,83-86,89,91,92,94
5 Jadad score	60%	72%	42%	28-35,43,44,50-54,58,63,64,67-71,73,74,78,80,82,87,88,90,93

5.3.3 Measurement of Frailty

Although in all studies the authors labeled their participants as "frail", only three studies utilized one of the validated operational definitions of frailty; Fried's frailty phenotype,[78] Speechley and Tinetti's Classification of Frailty and Vigorousness,[50-54] and Winograd's frailty scale.[90] In 12 studies non validated definitions of frailty were used.[20-38,58,60,62,63,72,73,75,76] These studies used a variety of outcome measures in an assortment of combinations to measure frailty.

Most studies (32 studies) did not include an operational definition of frailty. Although, nine studies mentioned at least one clinical marker of physical frailty (mobility and balance impairments, muscle weakness, testosterone deficiencies, and inactivity) in their inclusion criteria.[41,42,55-57,59,61,64,70,71,83,87,94] The inclusion criteria for the other 23 studies were; living in LTC,[45-49,69,77,79-81,84-86,88,91-93] or retirement home,[89] living in LTC or retirement home and experiencing ADL disability,[43,44,65,67,82] nursing home residents with incontinence,[68] physical restrained nursing home residents,[66] patients who could not leave their home by themselves referred by general practitioners,[39,40] older adults admitted to a hospital due to a fall or with a history of injurious falls that required medical treatment.[74]

Earlier stages of frailty were included in seven studies. Five studies[28-31,36-38,50-54,60,62] focused only on early stages of frailty whereas two studies[32-35,78] included one group at an early stage and another group at a later stage of frailty. The early stage of frailty was measured using different tools and was classified differently across studies as prefrail,[78] transitionally frail,[50-54] mild to moderate frail,[28-31,36-38,62] and moderately frail[32-

[35,60]. However, for the purpose of this review we will call these early stages of frailty as moderate frailty.

5.3.4 **Intervention Characteristics**

5.3.4.1 Frequency

The majority of the exercise interventions were performed either twice (11 studies)[20-27,39,40,50-57,72,73,77,78,84,89,91,94] or three times (27 studies)[28-38,41,42,45-49,58-63,65-67,69,71,74-76,80-82,88,90,92,93] per week. Two studies increased the exercise frequency to five times per week.[68,83] Two other studies did not report exercise frequency.[70,79]

5.3.4.2 Intensity

A detailed description of the exercise intensity was only provided for 18 of 47 studies[28-31,36-38,47-49,61,65,66,68,70-72,74,78,80-82,85,89,90] and five studies[39,40,58,75,88,91] offered no information regarding exercise intensity. In four studies the exercise intensity was evaluated using a perceived exertion scale.[20-27,61,64,87] Most of the interventions that utilized a resistance training program reported intensity as three sets of eight repetitions at approximately 80% of the individual's one repetition maximum (1RM).[36-38,47-49,70,71,80,81,90] Three resistance training programs compared low intensity (20 and 40% 1RM) to high intensity (80% 1RM) training and found that the changes in muscle strength and endurance were greater in the high intensity group compared with the low intensity.[70,71,80] However, improvements for functional ability were only marginally different, and ADL disability scores were similar between the two groups.

5.3.4.3 Duration

The duration of the interventions ranged from one[45,46,79] to 18 months[58] and the most common duration was three months.[39,40,43,44,59,61,62,65,70-74,81,84,86,88] The duration per session ranged from 10[84] to 90 minutes[55-57,78,94] and the majority of the studies included interventions that lasted either 45 minutes/session (six studies)[20-27,43,44,47-49,77,81,93] or 60 minutes/session (12 studies).[39-42,50-54,59,60,64,65,69,72,76,87,89] Fourteen studies did not report the duration of the exercise sessions.[36-38,62,63,66,68,70,71,74,79,80,82,85,88,90]

5.3.4.4 Type

Twenty-four studies[20-35,39,40,43,44,55-59,62,64,66-69,72-76,79,83,89,91,93,94] included multicomponent exercise interventions (usually focusing on resistance, balance, aerobic, and flexibility training), 14[36-38,41,42,47-49,60,61,63,65,70,71,77,80,81,90,92] resistance training, and seven other types of exercise interventions (walking exercise program,[85] balance training,[45,46] water exercises,[87] Tai Chi,[50-54] whole body vibration exercise,[82] exercise therapy using the Takizawa Program,[88] exercise using a horse-riding simulator[84]). However, each of these 'other' exercise interventions were included only in one study therefore conclusions regarding their individual effect cannot be made (table 5.5). In addition, two studies compared walking with balance training and reported that their effect on functional ability and adverse health consequences were similar.[78,86]

5.3.5 Methodological Quality

The total Jadad methodological quality score of the studies ranged from 1 to 5. Twenty-one studies[28-35,43,44,50-54,58,63,64,67-71,73,74,78,80,82,87,88,90,93] had perfect scores, four[20-27,41,42,61,91] scored 4, 13[45-49,55-57,59,65,66,72,75-77,86,89,92,94] scored 3, eight[36-40,60,62,81,83-85] scored 2, and one[79] scored 1. No studies were excluded on the basis of their quality score since one of the criteria of the scale was modified as described in the methods section. In 34 studies[20-35,43-59,63-65,67-78,80,82,86-90,92-94] the method of randomization was described, whereas 13 studies[36-42,60-62,66,79,81,83-85,91] reported randomized-controlled trials but the method of randomization was not described. Twenty-four studies[28-35,41-44,50-54,58,61,63,64,67-71,73,74,78,80,82,87,88,90,91,93] used a single-blinded design, two studies[20-27,66] used designs where not all outcome assessors were blinded to treatment allocation, six studies[72,75,77,85,86,89] were not blinded, and in 15 studies[36-40,45-49,55-57,59,60,62,65,76,79,81,83,84,92,94] the authors did not include any information regarding blinding of the outcome assessors. All but one study[79] included a description of withdrawals and dropouts (table 5.5).

5.3.6 **Exercise Compliance, Adverse Events, Cost**

Thirty-five of the 47 studies included information regarding exercise compliance.[20-35,39-57,61,64-67,69-78,80-82,86,87,89-94] In these studies the compliance to exercise sessions (exercise classes attended) for the intervention groups ranged from 42%[89] to 100%[28-31] and the mean compliance was 84%. From the seven studies[28-38,50-54,60,62,78] that included moderately frail adults, only four[28-35,50-54,78] reported exercise compliance rates and these were similar to the other studies (76%, 77%, 86%, 100%, respectively).

In 16 studies there were no adverse events during the period of the study or the adverse events were similar between the intervention and the control groups.[20-27,32-35,41-44,47-57,61,67,69,74,75,77,80,91,93,94] Latham et al.[90] reported that home-based high-intensity resistance exercise increased the risk of musculoskeletal injuries in frail people recently discharged from hospital. Eighteen out of 120 patients experienced episodes of back or knee pain that were directly attributable to the exercise. In another study, that focused on moderately frail people, two out of 66 exercise participants experienced musculoskeletal injuries (rotator cuff injury and worsening of an existing shoulder problem during resistance training); however, there were no other adverse events reported.[28-31] In 29 studies there was no discussion regarding adverse events during the period of the study.[36-40,45,46,58-60,62-66,68,70-73,76,78,79,81-89,92]

Three studies reported the cost of the exercise intervention.[32,55,67] Gill et al.[32] stated that six months of home-based physical therapy cost $1998 (US) per participant. Murlow et al.[67] reported that the cost per person for a 4-month exercise program in nursing homes was $1220 (US) and for friendly visits (control) was $189 (US). In another study[55] the cost per person (recently discharged from hospital) for the 10-week group exercise program was ~ $850 (US) and for the home exercise program was ~ $2280 (US).

5.3.7 **Outcome Measures**

5.3.7.1 Physical and Psychosocial Determinants

5.3.7.1.1 *Body Composition*

Body composition was tested in 12 studies[20,22-24,28-31,36,38,40,47,48,52,60,70-72,76,83] using seven outcome measures; weight,[22-24,28-30,36,38,47,52,70,72,83] BMI,[52,76,83] muscle mass,[20,22,24,29,30,36,38,40,47,60,70-72,76] muscle fiber distribution,[48,60] body fat mass,[24,29,40,70,83] bone mass,[24,31] arm and calf circumference.[83] Each outcome measure was tested using various tools (e.g. DEXA and MRI). Exercise improved body composition only in nine of the 31 cases that body composition as an outcome was tested. Specifically weight increased in two[22-24,70] of the eight studies, muscle mass increased in four[20,22,24,29,30,36,38,47] of the 10 studies, and fat mass was reduced in one[70] of five studies. BMI, muscle fiber distribution, bone mass, and arm and calf circumference did not improve in any study.

5.3.7.1.2 *Nutritional Status*

Nutritional status was reported in seven studies[20,22,23,26,27,29,47,70,72,76,83] and evaluated using two to three week daily food records to calculate energy, protein, carbohydrate and fat intake,[20,22,23,26,29,47,70,72,83] haematological indicators of nutritional status,[20,23,26,27,76,83] resting energy expenditure,[76] and sensory (smell, taste, hunger perception) performance and appetite.[20,22] Exercise improved dietary intake in three[20,22,47,83] of the six studies, protein intake in one[83] of two studies, hematological indicators in one[83] of three studies, and carbohydrate intake in the only study[22] where this outcome was tested. Fat intake, resting energy expenditure, blood nutrient, sensory performance and appetite did not change in the single study that evaluated these outcomes.

5.3.7.1.3 *Biochemical status*

Biochemical status was tested in seven studies measuring; immune parameters (e.g. tumor necrosis factor alpha expression and interleukin),[27,38,59,68,81] serum insulin-like growth factor-I (IGF-I),[49,60] markers of muscle regeneration and damage,[48,49] and muscle protein metabolism.[36-38] Exercise improved immune status in two studies,[27,38] did not have an impact on two other studies,[68,81] and had a negative impact (decreasing natural killer cell activity) in one study.[59] IGF-I improved in one of two studies where this outcome was measured.[49] Exercise improved markers of muscle regeneration[48,49] and muscle protein synthesis[36-38] whereas markers of muscle damage were similar between the exercise and the control group.[48,49]

5.3.7.1.4 *Cardiorespiratory Function*

Cardiorespiratory function was tested in four studies[28,30,39,40,52,68] using measurements of maximal oxygen consumption (VO_2max),[28,30,39,40] resting and exercise heart rate[30,52,68] and blood pressure,[30,52] cardiac output,[30] and left ventricular stroke volume.[30] Exercise had a significant impact on nine of the 11 studies that tested cardiorespiratory function. The only outcomes that did not change were resting heart rate and blood pressure in one[30] of the two studies[30,52] where these outcomes were measured.

5.3.7.1.5 *Muscle Function*

Muscle function was tested in 29 studies using a variety of tests.[28,29,36,38-43,47,48,56,60-63,65,66,68,70-72,74-77,80-83,89,90,92,93] Thirteen studies[41-43,47,48,56,60,61,63,76,80,81,89,90,92] tested only lower body muscle function, five studies[39,40,66,68,77,83] examined only upper body muscle function, 10 studies[28,29,36,38,62,70-72,74,75,82,93] investigated both lower and upper body muscle function, and one study[65] evaluated both lower and upper body, and trunk muscle function. Four studies[75,76,92,61] measured leg extension power and one study[80] included leg extension endurance. The remaining studies tested only muscle strength. Various muscles of the upper body and lower body were tested using different tasks (e.g. 1RM, isometric, isokinetic) and the most common muscles tested were the knee extension muscles.

Exercise training improved muscle function in the majority of studies. Only seven[65,70,75,76,82,89,90] of the 24 studies that measured lower body muscle function and three[65,74,82] of the 16 studies that measured upper body function did not show positive results and, the only study[65] that measured trunk strength was positive. Two of the four studies that measured leg extension power observed positive results.[61,92] Similarly, knee extension endurance was shown to improve in the one study where it was measured.[80]

5.3.7.1.6 *Flexibility*

Flexibility was examined in seven studies[62,65,66,77,82,88,93] by using various tests (range of motion around various joints,[62,65,66,77,88,93] back scratch test,[82] sit and reach test[82,93]). Two studies[62,65] measured lower and upper body, and trunk flexibility, three studies[82,88,93] measured lower and upper body flexibility, one study[77] measured lower body and trunk flexibility, and one study[66] measured only upper body flexibility. Exercise improved flexibility in the majority of the studies that measured this outcome. Lower body flexibility improved in four[62,65,88,93] of the six studies,[62,65,77,82,88,93] upper body flexibility improved in five[62,65,66,88,93] of the six studies,[62,65,66,82,88,93] and trunk flexibility improved in all three studies[62,65,77] that measured this outcome.

5.3.7.1.7 *Physical Activity Participation*

Levels of physical activity participation were assessed in seven studies[46,47,64,68,73,74,91] using activity monitors (motion sensors[68] and large scale integrated activity monitors[47]) interviews,[46,73] questionnaires,[64,74,91] and staff observations.[68] Exercise improved post-study daily physical activity levels in all seven studies that measured this outcome regardless of how it was measured.

5.3.7.1.8 *Neurological and Cognitive Function*

Neurological function was tested in four studies using visual stimulus reaction time,[26,62,89] auditory stimulus reaction time,[85] coordination,[26,62] and peripheral sensation (light touch and pressure sensation, and proprioception).[62] Exercise improved neurological function in three of eight cases when neurological function was tested as an outcome. More specifically exercise improved reaction time to visual stimulus in one[89] of the three studies, coordination in one[62] of the two studies, and reaction time to auditory stimulus in the only study that reported this outcome.[85] However, exercise did not affect peripheral sensation.[62] Cognitive function was measured in three studies[67,69,77] using the mini-mental status exam and improvement as a result of the exercise intervention was reported in only one[69] of these studies.

5.3.7.1.9 *Psychosocial State*

Depression was measured in four studies using the Geriatric depression scale[67,74,77] and the Zung self-rating depression scale.[57] Exercise reduced depression in half of the studies that measured this outcome.[57,77] Other psychosocial state outcomes measured in ten studies were; emotional status,[74] behavioural problems,[79] degree of fatigue,[90] tiredness due to mobility problems,[75] safety scores,[66] social involvement,[25] health belief model,[72] self-efficacy and satisfaction with exercise.[64,73,91] Exercise had a positive influence on reducing tiredness related to mobility problems,[75] behavioural problems,[79] safety scores,[66] and self-efficacy and satisfaction with exercise.[64,73,91] Exercise did not have an impact on emotional status,[74] social involvement,[25] and on the health belief model.[72] Exercise was reported to negatively influence self-perceived fatigue.[90]

5.3.7.2 Functional Ability

5.3.7.2.1 *Mobility*

Walking speed was measured in 20 studies using 10 different tests either at usual or fast speed.[33,35,39-43,47,52,56,61-63,72-76,84,85,90,92,93] The distance of the walking tests ranged from 2.4[43,61] to 20 meters.[41,42] The most common was the 10-meter walk test which was used in six studies.[49,40,56,63,72,75,85] Walking speed improved with exercise in 14 of 20 studies that measured this outcome.[33,35,39-41,43,47,52,56,61,63,73-75,84,92] Mobility endurance was tested using the 6-minute walking test in three studies[63,80,89] and by measuring the distance an individual could walk or move their wheel chairs during a standardized protocol in two studies.[66,68] Exercise improved walking endurance in three of the five studies that measured this outcome.[68,80,89] Wheeling endurance improved in both studies.[66,68] Mobility using the timed up-and-go test was measured in 10 studies[41,42,69,72,74,82,84,86,90,92,93] of which seven[42,69,74,82,86,92,93] reported improved mobility. Chair rising ability was tested in 15 studies using six different tests.[33,35,52,61,63,65,66,72,74-77,80,82,91,92] The most common tests were the three repetition chair stand[33,35,52,74,80] and the 30 second chair stands[66,72,82,92] and both protocols were used in four studies. Exercise improved the chair rising ability in 13 of 15 studies that measured this outcome.[33,35,52,61,63,65,72,74-77,80,91,92] Stair climbing ability was tested in eight studies using seven different protocols (e.g. number of steps, time, height, power).[41,42,47,72,74,76,80,86,93] Stair climbing ability improved in four of these studies.[47,72,74,80]

5.3.7.2.2 *Balance*

Balance was measured in 22 studies[28,39,41-43,45,46,52,53,56,61-63,65,69,72,74,75,77,84-86,89,90,93] using multiple positions stance time tests (e.g. one leg stance, parallel stance, semi-tandem stance),[28,41,42,52,53,61-62,72,74,75,84-86] Berg balance scale,[28,39,43,45,46,56,62,69,90,93] functional reach test,[52,63,74,84-86] postural sway,[45,46,63,65,77,89] and nine other protocols that each was used only once.[45,46,52,53,62,72,84,86,89] Exercise improved 28 of the 41 balance outcomes that were tested. Balance measured using the Berg balance scale improved in all studies, with the exception of one.[90]

5.3.7.2.3 *Functional Performance Test Batteries*

In 15 studies researchers used nine various test batteries to measure the functional performance of the participants.[21,27,28,33,35,61-63,67,69-71,74,75,78,82,86] The distribution of the functional performance test batteries across studies was as follows; Tinetti performance oriented mobility assessment (POMA),[33,35,74,78,82,86] Physical performance test,[28,33,35,62,69,75] aggregate functional performance test,[70,71] and other tests used only once.[21,27,28,61,63,67,78] Exercise improved the functional performance scores in 15 of 18 test batteries across 15 studies. All of the studies that used the Physical performance test and the POMA reported positive changes associated with exercise.

5.3.7.3 Adverse Health Consequences

5.3.7.3.1 *ADL Disability*

Activities of Daily Living (ADL) disability was measured in 16 studies[21,28,32,33,35,41,42,67,72,74,77,78,80,83,87,88,90,93,94] using 13 scales; Functional Independence Measure,[72,87,88,93] Barthel Index,[74,77,90] Katz Activities of Daily Living Scale,[63,83] Groningen Activity Restriction Scale,[41,42,78] and other scales used only once.[21,28,32,33,35,41,42,72,74,78,80,90,94] Exercise showed positive results in reducing ADL disability in seven of the 16 studies that measured this outcome.[32,33,35,77,78,80,83,87,93] More specifically, in the 10 studies[32,33,63,72,74,77,83,87,88,90,93] that used Basic ADL (BADL) scales only half[32,33,77,83,87,93] showed positive effects, in the four studies[35,72,74,90] that used Instrumental ADL (IADL) scales only one[35] improved IADL ability, and in the six studies[21,28,41,42,78,80,94] that used both sub-scales only two[78,80] reported significant improvements.

5.3.7.3.2 *Quality of Life*

Quality of life was measured in ten studies[25,28,39,40,54,63,67,73,75,87,90] using five questionnaires; Medical Outcomes Survey Short-Form 36 (SF-36) questionnaire,[28,39,40,63,73,87,90] self-rated health status,[25,54,75] Sickness Impact Profile,[54,67] Dutch scale of subjective wellbeing for older persons,[25] EQ-5D questionnaire.[75] Exercise improved quality of life in four[28,39,40,73,87] of the 10 studies that measured this outcome. The questionnaire that was used in all positive studies was the SF-36.

5.3.7.3.3 *Falls*

Falls were examined in 11 studies[33,44,46,50,51,55,63,74,78,85,89,90] by testing; falls incident rates during or following an intervention,[44,46,50,55,74,78,85,89,90] time to first fall,[85,90] fear of falling,[33,46,51,63,74,90] walking steadiness,[74] and post-fall emotional state.[74] Exercise reduced falls incidence in two[46,89] of nine studies that measured this outcome whereas, in seven studies[44,50,55,74,78,85,90] the risk for becoming a faller was similar between the exercise and the control group. Similarly, time to first fall was analogous between the exercise and control group in the two studies where it was measured.[85,90] Exercise had a positive impact on fear of falling in five of six studies[33,46,51,63,74] and on the walking steadiness and post-fall emotional state, in the only study[74] where they were measured.

5.3.7.3.4 *Utilization of Resources*

Utilization of resources was assessed in three studies.[32,55,67] Murlow et al.[67] reported that there was no difference in health care charges (mean $11398 (US) per person during the 4-months intervention) between the nursing home residents of the intervention and the control group. In another study the health and social welfare costs and the fall-related health care costs were similar between the exercise and control groups (mean ~ $12410 (US) per person one year following the intervention).[55] In addition, multicomponent training did not influence admission to a nursing home nor the number of days spent in a nursing home.[32]

5.4 Discussion

This systematic review provides evidence that the term “frailty” was used extensively in relation to published exercise interventions. Most studies that examined the effect of exercise on frail people were published in the last decade and included primarily the oldest old (≥ 80 years old) female participants. Only 32% of all studies included an operational definition of frailty and from these studies only three (6%) included a validated definition of frailty. Even among these studies, there was no agreement on the tools to measure frailty leading to large heterogeneity between the participants (e.g. various degrees of frailty). In most of the included studies the participants were identified as frail but no tools were used to diagnose frailty. As such, it is difficult to establish if indeed the participants of all studies were actually frail. In addition, there may be other studies with frail participants that were not included in this review as the authors did not identify their participants as frail. The most common exercise interventions for frail older adults included in this systematic review were multicomponent exercise programs performed three times per week for three months with each session lasting 60 minutes.

This systematic review provides evidence that exercise interventions have a positive impact on frail older adults. Even though the participants were frail, the exercise adherence was high and there were no adverse events in most reported studies, which support exercise as a safe and feasible intervention for this population. Exercise seems to benefit the oldest old, frail women more than younger frail men. This age-related difference may be explained by the fact that younger frail people may experience a ceiling effect on some outcome measures (BADL disability, mobility, balance etc.). The sex-related difference may be explained by the fact that baseline physical and functional ability is less in women compared to men[95] therefore, there is more room for exercise improvement by women.

Exercise seems to be more beneficial in frail people living in long-term care (LTC) facilities compared to the community. The evidence to support hospital and retirement home exercise interventions is currently insufficient. However, these studies suggest that hospitalized frail older adults and those living in retirement homes do not seem to benefit from exercise to the same degree as that experienced by persons residing either the community or in LTC. Exercise may be more beneficial in one type of setting and not the other as a result of ceiling or floor effects on some outcome measures. For example, community-dwelling frail adults are often relatively independent despite being frail, which would suggest that their ability to perform ADL would still be quite high. Therefore, exercise would not change ADL disability to the same degree as it would in those residing in LTC. In contrast, IADL will not change to the same degree in LTC populations as compared to community-dwellers since their IADL ability would likely be too low to show a meaningful change.

In the studies where an operational definition of frailty was included exercise seemed to be less effective in comparison to the studies that did not use definitions of frailty. Some of the studies that did not use a definition of frailty may have included people who were non-frail therefore their participants were more likely to be healthier and perhaps more responsive to exercise training due to greater overload. In addition, exercise seems to be more effective in the earlier stages of frailty compared to the later stages of frailty. People with a greater degree of frailty may not be able to exercise as long, as often and as hard versus people at an earlier stage of frailty; therefore, they may not benefit from exercise to the same degree as the latter group.

Multicomponent training was more positive on the functional ability and adverse health consequences of the frail people; however, resistance training alone had a greater positive effect on the physical and psychosocial determinants. However, most of the physical and psychosocial determinants that the resistance training studies included involved muscle function outcomes. These outcomes had greater improvements if the exercise program focused solely on resistance training. Interventions lasting longer than five months seemed to result in greater gains on the adverse health consequences of the frail people than shorter duration interventions. Interventions with frequencies of three times per week were more beneficial for all outcomes but the physical and psychosocial determinants showed the greatest changes. These differences likely occurred because frail adults need more time to reach a level of exercise that may engender health and fitness benefits. In addition, longer duration interventions had more drop-outs than shorter duration interventions since many frail people would experience severe health problems and/or not survive to complete a long intervention; therefore the results of the longer duration interventions are influenced by those survivors who are healthier. The duration for each session of exercise that seemed to be the most beneficial was 30-45 minutes. This is less than what is usually recommended for healthy older adults[11] perhaps, because frail people may fatigue easier. In addition, while frail people were able to exercise at higher intensities; low intensity exercise had a similar effect on the adverse health consequences.

None of the studies included in this systematic review used frailty as an outcome measure. The outcomes that were predominantly assessed were physical determinants and functional ability. There is good evidence that exercise improves cardiorespiratory function, muscle function, flexibility, physical activity participation, and functional ability of frail older adults. Presently there is only moderate evidence that exercise has a positive impact on psychosocial state, biochemical status, and adverse health consequences. Finally, there is little evidence to suggest that exercise positively influences body composition and nutritional status in frail people. Neurological and cognitive function and utilization of resources were not included as an outcome in a sufficient number of studies to make recommendations. Studies with perfect methodological quality (5 out of 5), in accordance with the Jadad criteria, had more favorable results than did lower quality studies. Those lower quality studies were likely more prone to bias (e.g. selection bias), which could make the exercise interventions less effective.

Our study is in agreement with the other systematic reviews that the most common exercise protocol for frail older adults is multicomponent training performed three times per week, and that there is good evidence to support exercise training for improving function, but the evidence is not as strong for improving ADL disability.[15,16] In addition, the exercise recommendations for a healthy older adult are likely going to be different than those targeting frail older adults. Specifically, frail older adults may need long-term exercise programs with shorter duration sessions and a substantial balance component compared with healthy older adults.[11]

The results from the subgroup analysis (Table V) showed that selected factors had an impact on the effect of exercise on the management of frailty and should be taken in consideration. For example, the improvements from exercise were greater when the frail participants were 80-90 years compared with studies that included younger frail participants (71-79 years). Future studies examining the effect of exercise on frailty should consider these differences and not combine younger and older frail people within the same sample.

In conclusion, the recommendations made are based upon qualitative examination and should be interpreted with caution. Definitive conclusions regarding the beneficial effects of exercise intervention(s) on frailty should be determined with meta-analysis which was beyond the scope of this systematic review. Future systematic reviews should include only high quality studies (e.g. RCT) and focus solely on specific outcomes. Although this will limit the number of studies included within the review, it will improve homogeneity making meta-analysis more feasible.

Future study in this area should also strive to use one of the existing validated definitions of frailty to assess participants prior to classifying them as frail. There is a genuine need for more high quality studies on the effect of exercise on the psychosocial parameters and adverse health consequences. In addition, frailty should be used as an outcome measure in order to show if exercise can reverse frailty (frail reverse to non-frail) or if older people can transition from a greater state of frailty to a lesser state of frailty with exercise. Future studies should also include larger sample sizes, participants with various degrees of frailty, and should examine age- and sex- related differences of the benefits of exercise in frail older adults. More studies are also needed with various training protocols (type, duration, frequency, and intensity) in order to determine the most beneficial and safe protocol for this population.

5.5 Conclusion

The term “frailty” has been used widely in relation to exercise. Structured exercise training can have a positive impact on frail older adults and thus is helpful for the management of frailty. The most common exercise interventions that were summarized in this systematic review were multicomponent training interventions that lasted three months and were performed three times per week for one hour per session. However, longer-term multicomponent interventions with shorter duration sessions (30-45 min) might be a better option for this population; especially for the prevention of adverse health consequences. More high quality studies that use a validated definition of frailty, both as an inclusion criterion and as an outcome measure, and compare different participants’ and interventions’ characteristics are needed.

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CHAPTER 6

Discussion and Conclusions

6.1 Introduction

The concept of frailty is complex, due to the coexistence of physiological, psychological, and social factors that contribute to this geriatric syndrome. Measures of physical function are fundamental components of frailty that provide important information about identification and management of this syndrome. To our knowledge no previous studies have examined the association of frailty with physical function using multiple objective measures. The first aim of this thesis was to examine the physical function of older women across levels of frailty during performance-based tasks and throughout their normal daily life. To answer this objective this thesis examined the association of frailty with physical function within a community-dwelling cohort of older women from rural Greece (Chapters 2-4). The second aim of this thesis was to determine the impact of exercise on frail older adults through a comprehensive systematic review (Chapter 5). Four manuscripts address these aims (Chapters 2-5) and their primary findings are discussed below, followed by an explanation of the limitations for each study and suggestions for future research. Concluding comments related to the overall thesis are presented at the end of this chapter.

6.2 Physical Function During Performance-Based Tasks

6.2.1 The Association of Frailty with Physical Function During Performance-Based Tasks

The findings from Chapter 2 indicated that frailty, measured using the Frailty Index (FI),[1] was a better predictor of physical function than chronological age. Both frailty and chronological age were correlated with physical function but frailty had the stronger relationship. After adjustment for age, frailty remained correlated with physical function, thus the association of frailty with physical function cannot be explained solely by the influence of age.

Measures of physical function that best predicted frailty were ambulatory mobility (gait velocity, stride length, and 8-foot up-and-go) and lower body muscular endurance (30-second chair stands). There is strong evidence that lack of ambulatory mobility is associated with adverse health outcomes and it has recently been proposed as a strong criterion of frailty.[2,3] Ambulatory mobility is a complex task and will be affected more by frailty than other less complex tasks (e.g. handgrip strength). In addition, walking performance at preferred and maximal pace was strongly correlated with frailty. However, similar to our study Brown et al.[4] reported that walking at a preferred pace had a slightly stronger association with frailty than did walking at a faster pace. This may be related to frail older adults choosing a more stable walking pattern during their normal walking pace, perhaps as a protective measure to avoid falls.[5]

Lower and upper body muscular endurance was a better predictor of frailty than lower and upper body muscle strength. Muscular endurance is likely a stronger functional measure than strength because activities of daily living (ADL) typically do not require maximal effort but rather sustained submaximal effort.[6,7] Furthermore, isotonic muscle strength was a better predictor of frailty than isometric strength, the former measure being more relevant to physical performance during ADL.[8-10] Handgrip muscle fatigue was correlated with frailty whereas knee extension (KE) muscle fatigue was not.

The effect of age on muscle fatigue is equivocal due to various contraction types, protocol durations, and muscles studied.[11,12]

Dominant handgrip strength is frequently used as a criterion of frailty.[3,13,14] In this study dominant handgrip strength was related to frailty but this relationship was not as strong as isotonic dominant leg strength, lower body muscular endurance, and upper body muscular endurance. Brown et al.[4] also reported that lower body strength tests were more correlated with frailty than handgrip strength tests. In addition, poor knee extension strength is more related to subjective fatigue, a common criterion of frailty, than handgrip strength.[15] Non-dominant handgrip strength was better correlated with physical function than the dominant hand. Previous studies[16,17] reported that the non-dominant handgrip strength is more related to physical function and osteoporotic fractures than dominant hand. The cause of this discrepancy may be that healthy older adults use both hands equally,[18] but frail older adults may only use their dominant hand for ADL. Bonilhia et al.[19] reported that age-related changes in the dominant hand region of the brain were greater than the non-dominant hand region. In addition, another investigation has suggested that osteoarthritis was more prevalent in the non-dominant hand than the dominant hand[20] as an alternative and/or additive explanation for the relationship between hand dominance and frailty. Performance-based measures of physical function not only predict frailty but may also dissociate between levels of this geriatric syndrome.

6.2.2 **Physical Function During Performance-Based Tasks Across Levels of Frailty**

Physical function differed between levels of frailty, defined by tertiles, and there was accelerated decline in physical function beyond the intermediate FI tertile. The measures of physical function that discriminated lower and higher levels of frailty (less and more severe frailty) were; walking speed, stride length, lower body muscular endurance, and non-dominant handgrip strength. The decline in walking speed was steeper at the higher level of frailty whereas the decline in stride length, lower body muscular endurance and non-dominant handgrip strength was similar at the lower and higher levels of frailty. Dominant handgrip strength only discriminated between lower levels of frailty whereas isotonic KE strength, upper body muscular endurance, and agility only discriminated between higher levels of frailty. Frailty ranges from mild to severe,[21,22] and it is possible that lower levels of frailty might be associated with different factors from those observed in the higher levels of frailty.[13] Our results suggest that lower levels of frailty were more associated with changes in gait velocity and stride length during walking and lower body muscular endurance whereas higher levels of frailty were more associated with gait velocity, agility, and isotonic KE strength.

6.3 Physical Function During Daily Life

6.3.1 The Association of Frailty with Physical Activity

The findings from Chapter 3 indicated that convergent validity was strong between accelerometers and the other physical activity (PA) measures (Heart rate monitors, portable Electromyography, Global Positioning System, Minnesota Leisure Time Activity Questionnaire) but weaker when the other measures were compared among each other. Number of steps and duration of PA, measured using accelerometery, was more strongly related to frailty, measured using the FI, than the other measures. The measures of PA that were significantly different between tertiles were those assessed using accelerometry and the Minnesota Leisure Time Activity Questionnaire (MLTAQ).

However, the MLTAQ had a large floor effect for the older women who scored within the highest FI tertile.

Similar to our study, other reports correlate self-reported PA with objective measures of PA in older adults,[23-25] but objective measures were more strongly associated with health status.[24] Time spent in total activity ranged from 2.2-3.5 hours and time spent in moderate/vigorous activity ranged from 6-24 minutes. To our knowledge no other study has examined PA in Greek older adults using these objective measures. Studies using self-reported questionnaires were in agreement with our study that total and moderate/vigorous PA in Greece is quite low.

The total step and acceleration counts in this study were approximately half of that previously reported, even for those within the low FI tertile.[24,26,27] We recorded PA for 10 consecutive hours over a single day, compared with other studies that examine PA over 24 hours across multiple days. The mean acceleration counts per minute in community-dwelling Greek older women of this study were 48-153. Those participants who scored within low FI tertile recorded activity counts (153 counts/min) similar to those found in community-dwelling US older women above the age of 70 (170 counts/min)[28] but less than those found in Canadian active healthy older women (294 counts/min)[23] and slightly greater than those found in US older women at risk for mobility disability (132 counts/min)[25] and those residing in a nursing home (20-102 counts/min).[29] These differences are not surprising since we showed that mean acceleration counts decline with advanced frailty, making comparison between studies erroneous if the frailty level was dissimilar. The mean acceleration count recorded during a walking pace of 0.9 m/sec in older women is reported to be ~ 273 counts/min.[29] During physically active periods in our study, accelerometer counts were 210-340 counts/min and the average usual walking pace was performed at 0.9 m/sec. This result illustrates that the older women in this study spent most of their active time walking. The GPS speed found in a previous study[27] in older adults was 1.27 m/sec which is greater than the GPS speed reported in this study even for the low FI tertile (0.92 m/sec); however, our study included only women and we did not exclude participants who walked less than 10 minutes consecutively outdoors.

The duration of moderate/vigorous PA measured with accelerometers was correlated with self-reported PA duration despite self-reported PA duration being 3% greater. This finding is not surprising since most self-reports overestimate duration and intensity of PA, especially for moderate PA.[30] The moderate/vigorous PA minutes measured in this study with accelerometers were similar to those measured with the same device in US community-dwelling older women (6 min/day).[28] There were large, but non-significant, differences in time spent in PA between frailty tertiles when HR monitors were used to define intensity. This lack of statistical significance may be explained by the large variance seen in all PA measures and the smaller sample included for HR recordings. The current recommendation of a minimum of 30 minutes of moderate PA[31] was only achieved by; one woman as measured by accelerometer, four women as measured by HR monitor, and in 13 women when a self-report questionnaire was used as the measurement tool. Harris et al.[26] also found that when PA was recorded with accelerometers only 2.5% of the older adults (6/238) achieved recommended levels of PA. However, examining the association of frailty with current objective measures of

PA does not provide direct information on the intensity of muscular activity required to perform ADL in older women across levels of frailty.

6.3.2 The Association of Frailty with Muscle Activity

Electromyography (EMG) provides an indication of when muscle is active or resting[32] and enables determination of the duration of time spent in low, moderate, and high levels of muscle activity relative to maximum.[33] The findings from Chapter 3 indicated that EMG activity of the upper and lower body was correlated with both the FI and the PA as measured with accelerometry. Also, the percentage of time in which the muscles were active was similar to the percentage of accumulated PA throughout the day. Muscle activity of the upper body relative to the lower body had longer burst duration likely because older women spend a greater portion of the day seated or standing while they are doing housework. Thus, participation in daily life suggests that arm muscle movement is maintained relative to lower body ambulation. For example, frail older adults might engage more upper body movement relative to the lower body with ADL such as rising from a chair. This can be detected as greater muscle activity in the arm muscles compared with the thigh muscles. Many PA measures are not sensitive to this accumulation of PA. EMG is not meant to be a measurement tool for PA, but when low-threshold EMG bursts are assessed and used in combination with measures of gross movement such as accelerometers, it likely provides important information about upper body movements that cannot be gained from traditional lower body assessment. Ultimately, it offers a means to determine how hard the muscle is working while performing PA.

The findings from Chapter 4 indicated that the total duration that the muscles were active and quiescent was similar across all levels of frailty (non-frail, pre-frail, frail; measured with the Frailty Phenotype).[13] However, the characteristics of muscle activity and quiescence were different. Frail women activated their muscles fewer times but each muscle activation occurred over a longer duration compared with the non-frail women. In addition, muscle activity was greater in the arm muscles than the thigh muscles across all frailty groups and increased arm muscle activity was augmented in the triceps brachii. The muscles of the older women in this study were active 26-30% of the time (burst percentage) which is equal to ~ 2.5 hours. Other studies found longer[34] or shorter duration[33,35] of daily muscle activity compared to our study and these differences in muscle activity, beyond frailty status, may arise from experimental factors.

This study demonstrated that across all frailty groups thigh muscles were active 22% (~ 2 hours) and quiescent 50% (~ 4.5 hours) of the time. Compared to the thigh muscles the percentage of bursts was greater in the arm muscles. These results are consistent with a previous study in younger adults which reported that arm muscles are more active relative to thigh muscles.[35] The greater activity of the arm muscles compared with the thigh muscles (e.g. ~ 60% greater total duration of muscle activity) is likely because arm muscles relative to thigh muscles are not as strong[36] and they are needed extensively by older adults to execute ADL.[37] Due to differences in strength and types of use older women will need to engage arm muscles more than thigh muscles. Although arm muscles are not as strong as thigh muscles in both young and older adults, the age-related decline in strength is greater in the thigh muscles relative to arm muscles.[36,38-41]

Muscle activity and quiescence were similar in the two thigh muscles [vastus lateralis (VL), and biceps femoris (BF)] across all three frailty groups (non-frail, pre-frail, frail). In contrast, differences in muscle activity and quiescence were found between the two arm muscles [biceps brachii (BB), triceps brachii (TB)]. TB was active 39% of the time and quiescent 27% of the time; whereas BB was active 30% of the time and quiescent 41% of the time. Previous work in young adults indicated similarities in muscle activity between the lower limb muscles but not the upper limb muscles.[35] The observed differences between the two arm muscles in our study may be related to the greater strength of the BB compared with the TB and the greater usage of the TB for daily activities.

6.3.3 Muscle Activity Across Levels of Frailty

Although the total duration of muscle activity and quiescence was similar across all levels of frailty, independent characteristics of muscle activity and quiescence were different in the frail women compared with women experiencing lower levels of this syndrome (non-frail and pre-frail). The number of bursts observed in frail women was 28% fewer compared with the non-frail women, whereas there were 29% and 25% more EMG recorded gaps in frail women than non-frail and pre-frail women, respectively. This result suggests that muscle activity was less in frail women relative to non-frail and pre-frail women. Frail women were older and 77-85% less physically active (steps completed during the day) than non-frail and pre-frail women. PA was highly correlated with the number of bursts across all levels of frailty. Differences in chronological age and level of physical activity likely account for the limited muscle activity observed in the frailest older women.

Previous work in healthy mobile older adults has indicated that a reduction in the number of times that muscles were active is associated with an increase in the duration of each muscle burst.[42] Similarly, in our study burst number in frail women was less, but the duration of the bursts was longer. Specifically, mean burst duration of frail women was 26% longer than the non-frail women, while mean gap duration of frail women was 37% shorter compared with the pre-frail women. Fast velocity movements are more affected by aging than slow velocity movements,[7,38] which suggests that older frail women may move slower during ADL than younger non-frail and pre-frail women. Differences in rate of movement might contribute to the greater mean duration of muscle activity in frail women compared with the other two groups. The mean burst amplitude (amplitude of muscle activity each time muscles were active) was 36% less in the frail women compared with the pre-frail women. Frail women’s lower amplitude of muscle activity may be related to their lower level of PA since they may have participated in fewer tasks that would require the production of higher levels of force.

Muscle activity and quiescence discriminated higher levels of frailty, but only muscle activity characteristics discriminated between lower levels of frailty (differences in pre-frail women compared with the non-frail women). Each burst in pre-frail women was approximately 30% longer with 40% greater amplitude than the muscles of non-frail women. These two groups were of similar age, anthropometric and health characteristics, strength, and mobility. Factors such as impaired motor control and increased subjective fatigue, which are both outcomes of frailty, likely contribute to the differences in muscle activity.[22,43,44] Other physiological factors (e.g. muscle fiber-type proportion, motor unit firing rate, nerve conduction velocity, muscle fatigue) may also be related to differences between non-frail and pre-frail but studies have yet to examine the effect of frailty on these physiological characteristics and how exercise interventions may alter the effect of frailty on these characteristics.

6.4 Exercise and Frailty

The systematic review findings in chapter 5 indicate that the term "frailty" was used extensively in relation to published exercise interventions. Most studies that examined the effect of exercise on frail people were published in the last decade and included primarily the oldest old ($\geq$ 80 years old) female participants. Only 32% of all studies included an operational definition of frailty and from these studies only three (6%) included a validated definition of frailty. This systematic review provides evidence that exercise interventions can have a positive impact on frail older adults. Even though the participants were frail, the exercise adherence was high and there were no adverse events reported in most studies, which supports exercise as a safe and feasible intervention for this population. Exercise seems to benefit the oldest old, frail women more than younger frail men. This age-related difference may be explained by the fact that younger frail people may experience a ceiling effect on some outcome measures (ADL disability, mobility, balance etc.). The sex-related difference may be explained by the fact that baseline physical ability is less in women compared to men[45] and as such women have greater potential for exercise improvement.

Exercise seems to be more beneficial for frail people living in long-term care (LTC) facilities compared to those living in the community. The evidence to support hospital and retirement home exercise interventions is currently insufficient. These studies suggest that hospitalized frail older adults and those living in retirement homes do not seem to benefit from exercise to the same degree as that experienced by persons residing either in the community or in LTC. Exercise may be more beneficial in one type of setting and not the other as a result of ceiling or floor effects related to some of the outcome measures. In the studies where an operational definition of frailty was included exercise seemed to be less effective in comparison to the studies that did not use definitions of frailty. Some of the studies that did not use a definition of frailty may have included people who were non-frail therefore their participants were more likely to be healthier and perhaps more responsive to exercise training due to greater compliance to progressive overload principles. In addition, exercise seems to be more effective in the lower levels of frailty compared to the higher levels of frailty. People with higher level frailty may not be able to exercise as long, as often and as hard versus people at a lower level of frailty; therefore, they may not benefit from exercise to the same degree as the latter group.

Multicomponent training had a more positive effect on the functional ability and adverse health consequences of the frail people than resistance training which alone had a greater positive effect on both the physical and psychosocial determinants. However, most of the physical and psychosocial determinants that the resistance training studies included involved muscle function outcomes. These outcomes had greater improvements if the exercise program focused solely (specificity) on resistance training. Interventions lasting longer than five months seemed to result in greater gains on the adverse health consequences of the frail people than shorter duration interventions. Interventions with frequencies of three times per week were more beneficial for all outcomes but the physical and psychosocial determinants showed the greatest changes. These differences likely occurred because frail adults needed more time to reach a level of exercise that may engender health and fitness benefit. In addition, longer duration interventions had more drop-outs than shorter duration interventions since many frail people would experience severe health problems and/or not survive to complete a long intervention; therefore the results of the longer duration interventions may be influenced by those survivors who were likely healthier. The duration for each session of exercise that seemed to be the most beneficial was 30-45 minutes. This duration is less than what is usually recommended for healthy older adults[31], perhaps because frail people may fatigue easier. In addition, while frail people were able to exercise at higher intensities; low intensity exercise had a similar effect upon adverse health consequences.

None of the studies included in this systematic review used frailty as an outcome measure. The outcomes that were predominantly assessed were physical determinants and functional ability. There is good evidence that exercise improves cardiorespiratory function, muscle function, flexibility, physical activity participation, and functional ability of frail older adults. There is moderate evidence that exercise has a positive impact on psychosocial state, biochemical status, and adverse health consequences. Finally, there is little evidence to suggest that exercise positively influences body composition and nutritional status in frail people. There were an insufficient number of studies which addressed neurological and cognitive function and utilization of resources to make recommendations. Studies with perfect methodological quality, in accordance with the Jadad criteria,[46] had more favorable results than did lower quality studies. Those lower quality studies were likely more prone to bias (e.g. selection bias), which could make the exercise interventions less effective.

The most common exercise interventions for frail older adults were multicomponent exercise programs performed three times per week for three months with each session lasting 60 minutes. Our study is in agreement with the other systematic reviews that the most common exercise protocol for frail older adults is multicomponent training performed three times per week, and that there is good evidence to support exercise training for improving function, but the evidence is not as strong for improving ADL disability.[47,48] In addition, the exercise recommendations for a healthy older adult are likely going to be different than those targeting frail older adults. Specifically, frail older adults may require longer-term exercise programs with shorter duration sessions and a substantial balance component compared with the healthy older adults.[31]

6.5 Limitations

The studies described in Chapters 2-4 involved for reasons of practicality and feasibility a convenience sample of community-dwelling older women who were living in rural areas within the prefecture of Thessaloniki, Greece. Therefore, the findings of this thesis cannot be generalized to older men and women living in other countries and those living in Greek urban areas. However, the FI characteristics (median FI score 0.2; maximal FI score 0.6) reported from our convenience sample was similar to those reported in larger cohort studies from other countries (e.g. Canadian Study of Health and Aging, Australian Longitudinal Study on Aging) which suggests that our sample may be representative of the populations of other countries.[49-52] The operational definition used to assess frailty in Chapters 2 and 3 was the FI whereas the operational definition used in Chapter 4 was the Frailty Phenotype. The choice of the operational definition was based on the outcome measures of each study. The outcome measure in the studies included in

Chapter 2 was performance-based physical function and in Chapter 3 physical activity. Both of these measures are included in the Frailty Phenotype as frailty criteria; thus, this definition could not have been used to assess frailty in these studies. Using the outcome measures as frailty criteria would have overestimated the effect of frailty on them. In contrast, a FI could be developed independently of these measures. In addition, the FI is a more complex operational definition of frailty and we were only able to use it after our collaboration and training with Dr. Rockwood's research lab at Dalhousie University half way through this thesis.

The original sample size was 53 older women, however, three older women did not participate in the second day of testing therefore only 50 older women participated in the study of Chapter 3. From these 50 older women only 33 had complete EMG data across all muscles to be included in the study of Chapter 4. The sample size of these studies is small, thus data must be interpreted with caution. Even so, it was large enough to demonstrate the nature of the relationship between age and frailty. Frailty is clearly age-associated, but is not the same as chronological age.[53,54] For example, within this thesis a 63- and a 90- year old woman each had the same FI score (0.2; lower level of frailty), and frailty was only moderately correlated with chronological age. Although many measures of physical function were assessed, the association between frailty and most of these measures was significant. The power for the non-significant associations was low thus establishing a clinical association between these measures and frailty is premature, but a hierarchy of associations of frailty with all measures of physical function can be gained.

Result biases were possibly produced due to the physical function measures used in this thesis. Laboratory tests may provide more accurate findings about the physical function of older adults but some frail older adults are unable to attend a laboratory for testing due to their impaired health. Therefore, in order to examine physical function of women across levels of frailty only portable devices which allowed for the measurement of physical function during tasks and daily life in the home environment were included. Each PA measurement tool included in Chapter 3 has limitations. Self-report PA is the most readily accessible measure to gain information, but is influenced by fluctuations in health status, depression, fatigue and cognitive ability which are all common issues in frail older adults.[55] Activities that are most difficult to recall are the light to moderate activities,[56] which are typically most relevant in frail adults. In addition, walking which is the most important activity to measure in this population is unreliably assessed by questionnaire.[57] PA questionnaires designed for healthy older adults may be inaccurate when used with frail adults. The short version of the MLTAQ, used in this study, was not validated for older adults but was used for the development of the frailty phenotype in the Cardiovascular Health Study and subsequently used extensively for the measurement of PA in frail older adults.[13] The original MLTAQ was designed for a young population, is generalizable to men only, and valid for healthy older adults but mostly for the measurement of moderate intensity activities.[58] This questionnaire tends to focus more on moderate to vigorous activities,[59] illustrated through the large floor effect observed in the high FI group. Although this questionnaire is regularly used it may not be valid for the measurement of PA in frail adults. The Stanford 7-day Physical Activity Recall questionnaire likely offers greater representation of PA in frail older adults.[58,59]

Waist-mounted accelerometers which were found to have the strongest association with frailty compared to the other PA measurement tools, as suggested in Chapter 3, underestimate upper body movements. HR monitors and EMG devices could overcome this problem. Actigraph accelerometer step counts have been shown to be accurate for walking speeds above 0.9 m/s but less accurate for lower speeds,[27,60] thus the steps recorded in this study may have been underestimated, especially for the frail older women. Recording step counts with accelerometers is more accurate than pedometers for slower speeds and shorter distances.[60] HR monitors overestimate light activities,[61] which are common in older adults and especially in frail, and are influenced by factors such as temperature, emotional state, caffeine etc.[62] In addition, prescription medications would likely alter heart rate, thus known equations to estimate HRmax could not be used. However, the HR values within each participant were positively correlated with the accelerometer data regardless of medication use, thus these devices might be limited for exact estimation of HRmax, but useful for determination of overall PA level.

The findings from Chapter 3 about moderate/vigorous intensity PA must be interpreted with caution. Cut-off values to assess the time spent in different intensities of PA are unknown for frail older adults for any of the devices used in this study. Accordingly, we used the cut-off values proposed for healthy older adults. For example, 4 METS was the cut-off for moderate intensity for the MLTAQ, but 4 METS may be perceived as a light activity for healthy and very active older adults, but vigorous activity for a frail person. Thus, the duration of time spent in moderate activities for frail women in this study is likely underestimated. However, a recent study[63] found that the cut-off values for moderate activity measured with accelerometers are similar between young

(20-29 years), middle-aged (40-49) and older healthy adults (60-69 years). This suggests that there might be no need to create different cut-off values based on age. In addition, recommended levels of PA are based on self-report rather than accelerometers. Adherence to these recommendations is substantially lower when accelerometers are used as the measurement tool relative to self-report.[28] Thus, the recommended duration and intensity of PA to improve health will likely be lower if accelerometers are used as an assessment tool.

In the systematic review included in Chapter 5 only studies which were published in either English or French and whose study participants were identified as ‘frail’ in either the title, abstract and/or text were included. The language restriction may over- or under-estimate the effectiveness of exercise interventions for the management of frailty. In addition, in most of the included studies the participants were identified as frail but no tools were used to diagnose frailty. As such, it is difficult to establish if indeed the participants of all studies were actually frail. There may be other studies with frail participants that were not included in this review as the authors did not identify their participants as frail. Even among the studies that included an operational definition of frailty, there was no agreement on the tools to measure frailty leading to large heterogeneity between the participants (e.g. various levels of frailty). Due to this variability a meta-analysis could not be satisfactorily performed and only subgroup analysis was done.

6.6 Directions for Future Research

This thesis demonstrated that physical function during performance-based tasks and daily life differs across levels of frailty. However, due to our cross sectional design it is still unknown whether frailty is the cause or the effect of the changes in physical function. Future longitudinal studies may address this question and should extensively examine factors related to physical function difference across the levels of frailty and between sexes. Yet this may be exceedingly difficult with the oldest and frailest adults. In addition, extensive investigation is necessary to examine the role of dominance in physical function, especially whether differences exist between lower limbs, and to understand the role of fatigue relative to frailty rather than mere chronological age.

The findings of this thesis provide evidence that a combination of PA measurement tools may provide important information about the level of PA in older women across levels of frailty. Combining these methods in a single device with sensors in upper and lower body and trunk would simplify the synchronization of the data, reduce the cost of buying multiple devices, and improve the prediction of the intensity of the activity.[62] In addition, future research should examine whether the current recommendations for PA in healthy older adults (minimum of 30 minutes, progressing to 60 minutes, of moderate intensity activity on most days of the week)[31] are applicable for frail adults and whether the type, intensity and time (net acquisition over day or singular bout) of PA is of relevance for this population in order to improve health and fitness.

There is evidence in the literature about PA questionnaires that can be used to measure the PA of healthy older adults but research is needed to examine which PA questionnaire is most appropriate for frail older adults and establish an effective recall period (days, weeks, months) that may best suit this population. It is recommended that healthy older adults wear PA devices for a minimum of three days and encompass weekdays and weekends to enhance accuracy of measurement.[64] However, some devices like GPS have limited time-logging allowing for less than nine hours of recording. Frail older adults are less active and may have less variance in their activities across days;[23] thus, future research should not only examine the appropriate device but also the recording period.

The self-report questionnaire in this thesis provided information on the type of PA performed and the GPS established if the PA was done outside, but all other objective measures could not provide information on the type of PA performed by these older women. Ongoing surveillance, either by shadowing the person or by video camera could objectively measure types of PA but both methods also have limitations in that they might influence task performance due to the recording area and would likely sway personal life space habits. Future studies that will measure objectively the types of PA performed during the day without affecting the daily life of older adults across levels of frailty are needed. In addition, these studies should examine how older adults activate arm and thigh muscles to perform ADL.

Future studies on the impact of exercise on frailty should strive to use one of the existing validated definitions of frailty to assess participants prior to classifying them as frail. There is a genuine need for more high quality studies on the effect of exercise on the psychosocial parameters and adverse health consequences. In addition, frailty should be used as an outcome measure in order to show if exercise can reverse frailty (frail reverse to non-frail) or if older people can transition from a greater state of frailty to a lesser state of frailty with exercise. Future studies should also include larger sample sizes, participants with various levels of frailty, and should examine age- and sex- related differences of the benefits of exercise in frail older adults. More homogeneous studies are also needed with various training protocols (type, duration, frequency, and intensity) in order to conduct a meta-analysis on the most beneficial and safe protocol for this population.

6.7 Conclusion

Frail older adults experience impairments in many domains of physical function during daily life and performance-based tasks, thus definitions of frailty need to combine various physical function measures targeted for the management of frailty.[22] This thesis examined numerous measures of physical function believed to be associated with frailty and whether structured exercise programs should be used for the management of frailty. The useful predictors of frailty during performance-based tasks identified were ambulatory mobility, lower body muscular endurance, and non-dominant handgrip strength. In addition, multiple methods can be used to accurately determine the duration and intensity of PA in older adults across levels of frailty since each method examined in this study had limitations but provided useful information about different aspects of PA in this population. However, accelerometers showed good agreement with the other PA methods, had the strongest association with frailty, and could be used to dissociate levels of frailty. Muscle activity and quiescence, as measured by portable electromyography, may add additional insight to the dissociation of frailty since they differ across levels of frailty. Beyond the use of muscle activity and quiescence to dissociate levels of frailty, they may also be used to indicate differences between the upper and lower body muscles. Finally, the systematic review indicated that structured exercise training can have a positive effect on the frail older adults and thus can be helpful for the management of frailty. There was a paucity of evidence to characterize the most beneficial exercise program for this population. However, multicomponent training interventions, of long duration (≥ 5 months), performed three times per week, for 30-45 minutes per session, generally had superior outcomes than other exercise programs.

The findings from this thesis that focused on older women indicated that the criteria selected to define frailty and the measurement protocols for these criteria are important. Definitions of frailty need to combine measures that can identify impairments in various domains of physical function during tasks and daily life. Future investigations will help classify the potential role of these measures in preventing further functional decline as well as human and economic burden associated with the syndrome of frailty.

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Appendices

Appendix A
Health History Questionnaire (Chapters 2-4)

Adapted from:

Rogers ME. Preexercise and health screening. In: Jones JS, Rose DJ eds. Physical Activity Instruction of Older Adults. Champaign IL: Human Kinetics, 2005, pp 57-80.

Code: **Date:**

Name:					
Address:					
City		*State:*		*Zip:*	
Home Phone #:		*Gender:*	*Male* ☐	*Female* ☐	
Whom to contact in case of emergency:		*Phone #:*			
Date of Birth:					
Height:	________*m* ___________*in*	*Weight:*	________*kg* __________*lb*		
Country of birth:		*Ethnic background:*			
Length of Stay in the Country that you live now:					

1. Have you ever been diagnosed as having any of the following conditions?			**If Yes Year of Diagnoses**
Heart attack	☐Yes	☐No	________
Transient ischemic attack	☐Yes	☐No	________
Angina (chest pain)	☐Yes	☐No	________
High blood pressure	☐Yes	☐No	________
Stroke	☐Yes	☐No	________
Peripheral vascular disease	☐Yes	☐No	________
Diabetes	☐Yes	☐No	________
Neuropathies (problems with sensations)	☐Yes	☐No	________
Respiratory disease	☐Yes	☐No	________

Parkinson's disease	☐Yes	☐No	______
Multiple sclerosis	☐Yes	☐No	______
Polio/Post polio syndrome	☐Yes	☐No	______
Epilepsy/seizures	☐Yes	☐No	______
Other neurological conditions	☐Yes	☐No	______
Osteoporosis	☐Yes	☐No	______
Rheumatoid arthritis	☐Yes	☐No	______
Other arthritic conditions	☐Yes	☐No	______
Visual/depth perception problems	☐Yes	☐No	______
Inner ear problems / Recurrent ear infections	☐Yes	☐No	______
Cerebellar problems (ataxia)	☐Yes	☐No	______
Other movement disorders	☐Yes	☐No	______
Chemical dependency (alcohol and/or drugs)	☐Yes	☐No	______
Depression	☐Yes	☐No	______

2. Have you ever been diagnosed as having any of the following conditions?

Cancer ☐Yes ☐No

If YES describe what kind: ____

Joint replacement ☐Yes ☐No

If YES, how many times?

- ☐ **Right Hip**
- ☐ **Left Hip**
- ☐ **Right Knee**
- ☐ **Left Knee**

Cognitive disorder ☐Yes ☐No

If YES describe condition: ____

Uncorrected visual problems ☐Yes ☐No

If YES describe type: ____

Any other type of health problem? ☐Yes ☐No

If YES describe condition: ____

3. Do you currently suffer any of the following symptoms in your legs or feet?

Numbness	☐Yes	☐No
Tingling	☐Yes	☐No
Arthritis	☐Yes	☐No
Swelling	☐Yes	☐No

4. Do you currently have any medical conditions for which you see a physician regularly?

Yes ☐ No ☐

If YES, please describe the conditions(s):

____

5. Do you require eyeglasses? ☐Yes ☐No

If YES, what type of glasses do you wear?

- ☐ Bi-Focals
- ☐ Graded Lenses
- ☐ Magnification Only
- ☐ Tri-Focals

6. Do you require hearing aids? ☐Yes ☐No

If yes, which ear? ☐Left ☐Right ☐Both

7. Do you use an assistive device for walking? ☐Yes ☐No ☐Sometimes

If YES or SOMETIMES, what type of assistive device do you use?

- ☐Single-Point Cane
- ☐3-Point Cane
- ☐Quad Cane
- ☐Rolling Stand Walker
- ☐3-Wheel Walker w/Seat

8. List all medications that you currently take (including all "over-the-counter" and "alternative medicines")

Type of medication	*For what condition*

9. Have you required emergency medical care or hospitalization in the past year?
☐Yes ☐No

If YES, please list when this occurred and briefly explain why.

10. Have you ever had any condition or suffered any injury that has affected your balance or ability to walk without assistance? ☐Yes ☐No

If YES, please list when this occurred and briefly explain condition or injury.

11. How many times have you fallen __within the past year__? ____________

If yes, please list a detailed description of the incident:

(a) Date: ____________________

(b) Location (i.e. indoors, outdoors): ____________________

(c) Reason for fall (i.e. uneven surface, going downstairs):

(d) Did you require medical treatment? ☐Yes ☐No

12. Are you __worried__ about falling? (circle)

☐1 - - - - - ☐ 2 - - - - - ☐3 - - - - -☐ 4 - - - - - ☐5 - - - - - ☐6 - - - - - ☐7
not a little moderately very extremely

13. How would you describe your health (check)

☐Excellent ☐Very good ☐Good ☐Fair ☐Poor

14. In the past 4 weeks, to what extent did health problems limit your everyday physical activities (such as walking and household chores)?

☐Not at all ☐Slightly ☐Moderately ☐Quite a bit ☐Extremely

15. How much "bodily pain" have you generally had during the past 4 weeks? (While doing <u>normal activities of daily living)</u>:

☐None ☐Very little ☐Moderate ☐Quite a bit ☐Severe

16. In general, how much depression have you experienced within the past 4 weeks?

☐Not at all ☐Slightly ☐Moderately ☐Quite a bit ☐Extremely

17. In general, how would you rate the quality of your life? (Circle the appropriate number)

☐1 - - - - - ☐ 2 - - - - - ☐3 - - - - -☐ 4 - - - - - ☐5 - - - - - ☐6 - - - - - ☐7

very low low moderate high very high

18. Please indicate you ability to do each of the following (*check appropriate response*).

	Can Do	**Can Do with difficulty or with help**	**Cannot Do**
a. Take care of own personal needs – like dressing yourself If you answered "Can Do with difficulty or with help" OR "Cannot Do", why? ☐ Health problems ☐ Chronic pain ☐ Lack of strength or endurance ☐ Lack of flexibility or balance ☐ Other reasons: ________________________________	☐2	☐1	☐0
b. Bathe yourself, using tub or shower If you answered "Can Do with difficulty or with help" OR "Cannot Do", why? ☐ Health problems ☐ Chronic pain ☐ Lack of strength or endurance ☐ Lack of flexibility or balance ☐ Other reasons: _______________________________	☐2	☐1	☐0

c. Climb up and down a flight of stairs (like to a second story in a house) ☐2 ☐1 ☐0

If you answered “Can Do with difficulty or with help” OR “Cannot Do”, why?

☐ Health problems
☐ Chronic pain
☐ Lack of strength or endurance
☐ Lack of flexibility or balance
☐ Other reasons: ______________________________

d. Walk outside one or two blocks ☐2 ☐1 ☐0

If you answered “Can Do with difficulty or with help” OR “Cannot Do”, why?

☐ Health problems
☐ Chronic pain
☐ Lack of strength or endurance
☐ Lack of flexibility or balance
☐ Other reasons: ______________________________

e. Do light household activities – like cooking, dusting, washing dishes, sweepinga walkway ☐2 ☐1 ☐0

If you answered “Can Do with difficulty or with help” OR “Cannot Do”, why?

☐ Health problems
☐ Chronic pain
☐ Lack of strength or endurance
☐ Lack of flexibility or balance
☐ Other reasons: ______________________________

f. Do own shopping for groceries or clothes ☐2 ☐1 ☐0

If you answered “Can Do with difficulty or with help” OR “Cannot Do”, why?

☐ Health problems
☐ Chronic pain
☐ Lack of strength or endurance
☐ Lack of flexibility or balance
☐ Other reasons: ______________________________

g. Walk ½ mile (6-7 blocks) ☐2 ☐1 ☐0

If you answered "Can Do with difficulty or with help" OR "Cannot Do", why?

- ☐ Health problems
- ☐ Chronic pain
- ☐ Lack of strength or endurance
- ☐ Lack of flexibility or balance
- ☐ Other reasons: ________________________________

h. Walk 1 mile (12-14 blocks) ☐2 ☐1 ☐0

If you answered "Can Do with difficulty or with help" OR "Cannot Do", why?

- ☐ Health problems
- ☐ Chronic pain
- ☐ Lack of strength or endurance
- ☐ Lack of flexibility or balance
- ☐ Other reasons: ________________________________

i. Lift and carry 10 pounds (full bag of groceries) ☐2 ☐1 ☐0

If you answered "Can Do with difficulty or with help" OR "Cannot Do", why?

- ☐ Health problems
- ☐ Chronic pain
- ☐ Lack of strength or endurance
- ☐ Lack of flexibility or balance
- ☐ Other reasons: ________________________________

j. Lift and carry 25 pounds (medium to large suitcase) ☐2 ☐1 ☐0

If you answered "Can Do with difficulty or with help" OR "Cannot Do", why?

- ☐ Health problems
- ☐ Chronic pain
- ☐ Lack of strength or endurance
- ☐ Lack of flexibility or balance
- ☐ Other reasons: ________________________________

k. Do most heavy household chores – like scrubbing floors vacuuming, raking leaves ☐2 ☐1 ☐0

If you answered "Can Do with difficulty or with help" OR "Cannot Do", why?
- ☐ Health problems
- ☐ Chronic pain
- ☐ Lack of strength or endurance
- ☐ Lack of flexibility or balance
- ☐ Other reasons: ______________________________

l. Do strenuous activities – like hiking, digging in garden, moving heavy objects, bicycling, aerobic dance exercises, strenuous calisthetics, etc. ☐2 ☐1 ☐0

If you answered "Can Do with difficulty or with help" OR "Cannot Do", why?
- ☐ Health problems
- ☐ Chronic pain
- ☐ Lack of strength or endurance
- ☐ Lack of flexibility or balance
- ☐ Other reasons: ______________________________

19. In general, do you currently require household or nursing assistance to carry out daily activities?

☐Yes ☐No

If yes, please check the reasons(s)?
- ☐ Health problems
- ☐ Chronic pain
- ☐ Lack of strength or endurance
- ☐ Lack of flexibility or balance
- ☐ Other reasons: __________________________

20. **In a typical week, how often do you leave your house? (to run errands, go to work, go to meetings, classes, church, social functions, etc.)**

☐less than once/week ☐3-4 times/week
☐1-2 times/week ☐most every day

21. Do you <u>currently</u> participate in regular physical exercise (such as walking, sports, exercise classes, house work or yard work) that is strenuous enough to cause a noticeable increase in breathing, heart rate, or perspiration? ☐Yes ☐No

If yes, how many days per week?

☐One ☐Two ☐Three ☐Four ☐Five ☐Six ☐Seven

22. When you go for walks (if you do), which of the following best describes your walking pace:

☐Strolling (easy pace, takes 30 min. or more to walk a mile)
☐Average or normal (can walk a mile in 20-30 minutes)
☐Fairly brisk (fast pace, can walk a mile in 15-20 minutes)
☐Do not go for walks on a regular basis

23. In the last year, have you lost more than 10 pounds unintentionally (i.e., not due to dieting or exercise)? ☐ Yes ☐No

24. How often in the last week did you feel that everything you did was an effort

☐ Rarely or none of the time (<1 day) ☐ Some or a little of the time (1–2 days)

☐ Moderate amount of the time (3–4 days) ☐ Most of the time

25. How often in the last week did you feel that you could not get going

☐ Rarely or none of the time (<1 day) ☐ Some or a little of the time (1–2 days)

☐ Moderate amount of the time (3–4 days) ☐ Most of the time

26. How easily have you got tired over the last 2 weeks?

☐Not at all ☐Slightly ☐Moderately ☐Very ☐Extremely

27. How much have you been bothered by fatigue over the last 2 weeks?

☐Not at all ☐A little ☐A moderate amount ☐Very much ☐An extreme amount

28. Place a mark along the line to indicate your current fatigue level

No Fatigue |--| Worst Possible Fatigue

29. Do you feel tired after you perform the following activities?

a. Transfer	☐ Yes	☐ No
b. Walk indoors	☐ Yes	☐ No
c. Go outdoors	☐ Yes	☐ No
d. Walk outdoors in nice weather	☐ Yes	☐ No
e. Walk outdoors in poor weather	☐ Yes	☐ No
f. Climb stairs	☐ Yes	☐ No

30. Level of education:

- ☐ No schooling
- ☐ Primary
- ☐ High school
- ☐ Intermediate between high School and university (Technical school)
- ☐ University or college
- ☐ Masters
- ☐ Doctorate

☐ Some ☐ Completed

31. How many years have you spent at school or in full time study? ____________

32. Marital status:

☐ Married ☐ Widowed ☐ Separated ☐ Single

33. Children: ☐ Yes ☐ No If yes how many? ____________

34. Current living arrangement:

☐ Alone ☐ With spouse ☐ With children
☐ With sibling ☐ With in law/parent ☐ With other relative

35. Current work status:

☐ Fulltime ☐ Part time ☐ Looking for work ☐ Can't work ☐ Retired

36. Main type of employment during working life: ___________________________

37. Current financial status:

a) Are you comfortable with your financial situation at the moment? ☐ Yes ☐ No

b) Are you able to save money after all the expenses? ☐ Yes ☐ No

c) At the present time do you feel that you will have enough money for your expenses and needs in the future? ☐ Yes ☐ No

Appendix B
Short Version of the Minnesota Leisure Time Activity Questionnaire (Chapters 2-4)

Adapted from:
Taylor HL, Jacobs DR Jr, Schucker B, Knudsen J, Leon AS, Debacker G. A questionnaire for the assessment of leisure time physical activities. J Chronic Dis 1978;31(12):741-55.

ACTIVITY	**Did you perform this activity in the last 2 weeks?**		**How many times did you do this activity in the last 2 weeks?**	**How long did you usually do the activity each time?**	
	NO	**YES**		**Hrs**	**Min**
Walking for exercise					
Moderately strenuous household chores					
Mowing the lawn					
Raking the lawn					
Gardening					
Hiking					
Jogging					
Biking					
Exercise Cycle					
Dancing					
Aerobics					
Bowling					
Golf					
Single Tennis					
Doubles Tennis					
Racquetball					
Calisthenics/Weights					
Swimming					

Appendix C
Frailty Index: Domains, Measures and Scores (Chapters 2-3)

Table C.1. Domains, Measures and Scores for the Frailty Index for Chapter 2

Domain	Measure	Score
Comorbidities	(1) Cardiovascular disease; (2) Peripheral vascular disease; (3) Diabetes; (4) Respiratory disease; (5) Stroke; (6) Osteoporosis; (7) Arthritis; (8) Joint Replacement; (9) Vision Problems; (10) Hearing problems; (11) Cancer; (12) Cognitive Disorders; (13) Depression; (14) Arrhythmia; (15) Vertigo; (16) High Cholesterol; (17) High Glucose;	Yes = 1, No = 0
Leg/Feet Symptoms	(18) Numbness; (19) Tingling; (20) Swelling	Yes = 1, No = 0
General Health Status	(21) Hospitalization in past year; (22) >2 falls in past year	Yes = 1, No = 0
	(23) Self rating of health (scale: Excellent, Very Good, Good, Fair, Poor)	Poor = 1, Fair = 0.75, Good = 0.5, Very good = 0.25, Excellent = 0
	(24) Fear of falling (1-7 scale) (scale: 1 not, 2, 3, 4, 5, 6, 7 extremely)	7 = 1, 6 = 0.83, 5 = 0.67, 4 = 0.5, 3 = 0.33, 2 = 0.17, 1 = 0
Quality of life	(25) Self rating of Quality of life (1-7 scale) (scale: 1 very low, 2, 3, 4, 5, 6, 7 very high)	1 = 1, 2 = 0.83, 3 = 0.67, 4 = 0.5, 5 = 0.33, 6 = 0.17, 7 = 0
Mobility	(26) Using assistive device for walking	Yes = 1, No = 0
	(27) Walking pace	Strolling = 1, Average = 0.5, Fairly brisk = 0
Nutrition	(28) Lost more than 5 kg in the past year	Yes = 1, No = 0

(Table C.1 continued pg.193)

Table C.1. (Continued)

Domain	Measure	Score
Functional Independence	(29) Take care of personal needs; (30) Bathing; (31) Climb stairs; (32) Walk 1-2 blocks; (33) Walk 6-7 blocks; (34) Do own shopping for groceries or clothes; (35) Lift and carry a full bag of groceries; (36) Do light household activities; (37) Do most heavy household activities	Cannot do = 1, Can do with help = 0.5, Can do = 0
	(38) Overall function in Activities of Daily Living (0-24 score)[1]	<16 = 1, ≥16 = 0
	(39) Limitations in Activities of Daily Living due to health problems	Extremely = 1, Quite a bit = 0.75, Moderately = 0.5, Slightly = 0.25, Not at all = 0
Physical Activity	(40) Leisure Time Physical Activity Questionnaire[2]	<270 Kcals/week = 1, ≥270 Kcals/week = 0
Mood and Subjective Fatigue	(41) Bodily pain; (42) Feel depressed; (43) Feel Easily tired; (44) Bothered by fatigue 1 2 3 4 5 6 7 not at all … extremely	Extremely = 1, Quite a bit = 0.75, Moderately = 0.5, Slightly = 0.25, Not at all = 0
	(45) Feel Everything is an effort; (46) Have trouble getting going	Every day = 1, 3-4/week = 0.67, 1-2/week = 0.33, <1/week = 0
	Feel tired after: (47) Transfer; (48) Walk indoors; (49) Go outdoors; (50) Walk outdoors	Yes = 1, No = 0
Education	(51) Completed primary school	No = 1, Yes = 0

(Table C.1 continued pg.194)

Table C.1. (Continued)

Domain	Measure	Score
Social	(52) Living alone	No = 1, Yes = 0
	(53) Leave the house (for errands, work, church etc.)	<1/week = 1, 1-2/week = 0.67, 3-4/week = 0.33, Every day = 0
Financial Status	(54) Feeling comfortable with financial Status; (55) Able to save money after all expenses; (56) Have enough money for the needs in the future	No = 1, Yes = 0

kg, kilograms; **Kcal**, kilocalorie

[1]Rikli RE, Jones JC. The reliability and validity of a 6-minute walk test as a measure of physical endurance in older adults. J Aging Phys Act 1998;6:363-375.

[2]Fried LP, Tangen CM, Walston J et al. Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56(3):M146-M156.

Table C.2. Domains, Measures and Scores for the Frailty Index for Chapter 3

Domain	Measure	Score
Comorbidities	Cardiovascular disease Peripheral vascular disease Diabetes Respiratory disease Stroke Osteoporosis Arthritis Joint Replacement Vision Problems Hearing problems Cancer Cognitive Disorders Depression Arrhythmia Vertigo High Cholesterol High Glucose	Yes = 1, No = 0
Leg/Feet Symptoms	Numbness Tingling Swelling	Yes = 1, No = 0
General Health Status	Hospitalization in past year >2 falls in past year	Yes = 1, No = 0
	Self rating of health	Poor = 1, Fair = 0.75, Good = 0.5, Very good = 0.25, Excellent = 0
	Fear of falling (1-7 scale)	7 = 1, 6 = 0.83, 5 = 0.67, 4 = 0.5, 3 = 0.33, 2 = 0.17, 1 = 0

(Table C.2 continued pg.196)

Table C.2. (Continued)

Domain	Measure	Score
Quality of life	Self rating of Quality of life (1-7 scale)	1 = 1, 2 = 0.83, 3 = 0.67, 4 = 0.5, 5 = 0.33, 6 = 0.17, 7 = 0
Mobility	Using assistive device for walking	Yes = 1, No = 0
	Walking pace	Strolling = 1, Average = 0.5, Fairly brisk = 0
Nutrition	Lost more than 5 kg in the past year	Yes = 1, No = 0
Functional Independence	Take care of personal needs Bathing Climb stairs Walk 1-2 blocks Walk 6-7 blocks Do own shopping for groceries or clothes Lift and carry a full bag of groceries Do light household activities Do most heavy household activities	Cannot do = 1, Can do with help = 0.5, Can do = 0
	Overall function in Activities of Daily Living (0-24 score)[1]	<16 = 1, ≥16 = 0
	Limitations in Activities of Daily Living due to health problems	Extremely = 1, Quite a bit = 0.75, Moderately = 0.5, Slightly = 0.25, Not at all = 0

(Table C.2 continued pg.197)

Table C.2. (Continued)

Domain	Measure	Score
Mood and Subjective Fatigue	Bodily pain Feel depressed Feel Easily tired Bothered by fatigue	Extremely = 1, Quite a bit = 0.75, Moderately = 0.5, Slightly = 0.25, Not at all = 0
	Feel Everything is an effort Have trouble getting going	Every day = 1, 3-4/week = 0.67, 1-2/week = 0.33, <1/week = 0
	Feel tired after: Transfer, Walk indoors, Go outdoors, Walk outdoors	Yes = 1, No = 0
Education	Completed primary school	No = 1, Yes = 0
Social	Living alone	No = 1, Yes = 0
Financial Status	Feeling comfortable with financial Status Able to save money after all expenses Have enough money for the needs in the future	No = 1, Yes = 0
Handgrip Muscle Strength	The highest of three consecutive maximal handgrip strength measures of the dominant hand using a Jamar® hand-held dynamometer.[3]	≤17kg (BMI ≤ 23); ≤17.3kg (BMI 23.1–26); ≤18kg (BMI 26.1–29); ≤21kg (BMI >29) strength = 1

(Table C.2 continued pg.198)

Table C.2. (Continued)

Domain	Measure	Score
Upper Body Muscular Endurance	30-sec Arm Curl test (5 lb dumbbell)[2]	≤11 = 1, >11 = 0
Lower Body Muscular Endurance	30-sec Chair Stand test[2]	≤8 = 1, >8 = 0
Agility and Dynamic Balance	8-foot up-and-go test[2]	≥8.8 sec = 1, <8.8 sec = 0
Walking Speed	15-foot walk test at usual pace[3]	≥7 sec (Height≤159 cm); ≥6 sec (Height>159cm) = 1

kg, kilograms; **BMI**, Body Mass Index; **sec**, seconds; **lb**, pounds; **cm**, centimeters

[1]Rikli RE, Jones JC. The reliability and validity of a 6-minute walk test as a measure of physical endurance in older adults. J Aging Phys Act 1998;6:363-375.

[2]Rikli RE, Jones JC. *Senior Fitness test*. Champaign, IL: Human Kinetics; 2001.

[3]Fried LP, Tangen CM, Walston J et al. Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56(3):M146-M156.

Appendix D
Medline Search (Chapter 5)

1. frail elderly/
2. frail$ or pre-frail$ or prefrail$
3. or/1-2
4. exercise/ or exercise therapy/ or exercise tolerance/ or exercise test/
5. physical fitness/ or physical endurance/ or physical therapy/
6. rehabilitation/ or therapeutics/
7. sports/ or weight lifting/ or bicycling/ or running/ or swimming/ or walking/
8. leisure activities/ or recreation/
9. (physical adj3 (exercise$ or therap$ or conditioning or activit$ or fitness))
10. (exercise adj3 (train$ or intervention$ or protocol$ or program$ or therap$ or activit$))
11. (fitness adj3 (train$ or intervention$ or protocol$ or program$ or therap$ or activit$))
12. ((training or conditioning) adj3 (intervention$ or protocol$ or program$ or activit$))
13. (rehabilitation adj3 (exercise$ or train$ or intervention$ or protocol$ or program$ or therap$ or activit$))
14. (therapeutic adj3 (exercise$ or train$ or intervention$ or protocol$ or program$ or activit$))
15. (sport$ or recreation$ or leisure or cycl$ or bicycl$ or treadmill$ or run$ or swim$ or walk$)
16. ((endurance or aerobic or cardio$) adj3 (exercise$ or fitness or train$ or intervention$ or protocol$ or program$ or therap$ or activit$))
17. (muscle strengthening or progressive resist$)
18. ((weight or strength$ or resistance or power) adj3 (exercise$ or train$ or lift$))
19. ((balance or flexibility) adj3 (exercise$ or train$ intervention$ or protocol$ or program$ or activit$))
20. Tai Ji/ or yoga/
21. tai chi or yoga or pilates
22. or/4-21
23. 3 AND 22

Appendix E
Feedback to Participants: Report Card

NAME:

	SCORE	MEAN SCORE
STRENGTH LEGS (Repetitions)		
STRENGTH ARMS (Repetitions)		
HANDGRIP STRENGTH (RIGHT) (kg)		
HANDGRIP STRENGTH (LEFT) (kg)		
AGILITY (sec)		
WALKING AT NORMAL PACE (sec)		
WALKING AT MAXIMUM PACE (sec)		
AVERAGE HEART RATE DURING THE DAY (HEART RATE BEATS/MINUTE)		
STEPS		

TIME	STEPS	HR

TIME	STEPS	HR

TIME	STEPS	HR

Appendix F
Personal Framework: Self-Reflection on "Greek Older Women"

According to my experience, the Greek older women are very different than other women throughout the world. They are people who live for others. Their personal lives end long before death because they live through others, their children and their grandchildren. They are extraordinary people who carry a heavy past light-heartedly, offering unconditional love and support to their family.

Their everyday lives are simple and circular. They get up very early and they start doing housework, cooking, watch some television, lunch, siesta, television, *somporo*[a], and then go to sleep while their main hobby is going to church. The exceptions, which disrupt their routine, are very few including the bath, a visit to the doctor, medical tests, a family or community gathering, elections and national celebrations. Their life is not much different than the one they had in their 30s. The most extraordinary thing about this generation of women is the radical change in their lives when their husbands die. They mourn for the rest of their lives wearing black while following cultural restraints. They would even stop participating in happy family events, such as a child's baptism.

It is a generation of women who grew up living with the older adults in the family, who were authoritarian figures. However, when they grew old, things had changed dramatically to a point that what they said became less important, yet expected to facilitate with the care of younger generations.

This generation of Greek women is different than my generation. Few of these women finished elementary school because of the Second World War. It is the generation who experienced a world war, a civil war, a dictatorship, and the political languor of the recent years. They lived the actual events without, on the other hand, acknowledging the historical data such as the reason why these events occurred or when they happened. For instance, they may not know the actual beginning of the Second World War but what they do is when the village was full of Germans and how many years they lived with them. They do not know the official differences between the right and left ideologies but all of them belonged either to one or the other. Years later, this generation, who had to live with the black marketer and the traitor, tired of fighting compromised and learned to live with each other without ever mentioning the past.

[a] Social female gathering which usually takes place in the neighbourhood, either on a bench or in somebody's garden, in the evening time after the soap-operas have ended. One of the necessary presupposition is the clear visibility of the road so that the women will able to gossip whoever they see since one of the ordinary topics is usually the others people's lives, the actors' lives, and of course the reason for a neighbour's absence in the gathering that night.

It is a generation of women who married somebody who knew very little, who watches on television how much the world has changed and became a place where anybody may kill anybody, people take drugs, rape, lost values. Fear and disillusions created by the television make them feel repulse for a world they actually know very little about.

The Greek older women do not have their own identity, their own name. In English, they are called “older women”, “elderly”, “frail women”, “aged women”, Mrs Smith. In Greek, it is my grandmother, my friend’s grandmother, my aunt’s mother, my colleague’s grandmother, my neighbour’s mother, *Giorgena*[a]. The Greek older women do not have autonomy, they always belong somewhere. Most of them never moved to the third age, they simply grew in it from their youth. My grandmother has been the same since I remember her. However, not all of them are like that. There is Professor Arveler, Ms Zozo Sapoutzaki, Theopoula, Ms Melina Merkouri, Ms Aliki Vougiouklaki…and so many others who represent an old age with no limitations and cultural restraints in contrast to the women in my hometown who seem to have been born old accepting their condition unquestionably…this is how my grandmother, Elinas’ grandmother, Vassilis’ grandmother, Ms Litsa’s mother, *Patraklesina*[a] are….

[a] Very commonly the woman sometimes will be referred with the alternation of her husband’s first name instead of hers

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G.1a

"Theou O., Kloseck M. (2007). Tools to Identify Community-Dwelling Older Adults in Different Stages of Frailty. Physical and Occupational Therapy in Geriatrics Journal, 26(3):1-21."

Title:	Tools to Identify Community-Dwelling Older Adults in Different Stages of Frailty
Author:	Olga Theou et al.
Publication:	Physical & Occupational Therapy In Geriatrics
Publisher:	Informa Healthcare
Date:	Jan 1, 2007

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Volume number: 33
Issue number: 4
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Requestor type: Author (original work)
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Subject	**RE: Permission Request for manuscript**
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Date	Thursday, May 20, 2010 4:48 pm
To	Olga Theou

Dear Ms. Theou,

Dr. Rosenberg informs me that you would be able to include the manuscript in your PhD dissertation, but only if you currently describe it as "under review".

I hope this helps.

Sincerely,
Leah

Leah Timmermann
Research Assistant/Aide de Recherches
Dr. Mark Rosenberg, Editor-in-Chief/Rédacteur en Chef
Canadian Journal on Aging/Revue Canadienne du Vieillissement

Appendix H
Ethics Approval (Chapters 2-4)

Western

Office of Research Ethics

The University of Western Ontario
Room 4180 Support Services Building, London, ON, Canada N6A 5C1
Telephone: (519) 661-3036 Fax: (519) 850-2466 Email: ethics@uwo.ca
Website: www.uwo.ca/research/ethics

Use of Human Subjects - Ethics Approval Notice

Principal Investigator: Dr. A.A. Vandervoort
Review Number: **15332E** **Review Level:** Expedited
Review Date: July 23, 2008
Protocol Title: Comparison of physical activity and muscle function between Greek and Canadian older women
Department and Institution: Physical Therapy, University of Western Ontario
Sponsor:
Ethics Approval Date: September 5, 2008 **Expiry Date:** August 31, 2010
Documents Reviewed and Approved: UWO Protocol, Letter of Information and Consent, Advertisement.
Documents Received for Information:

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced study on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

[redacted]

Chair of HSREB: Dr. Paul G. Harding

[redacted]

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Curriculum Vitae

Olga Theou

EDUCATION

2006-2010	Doctor of Philosophy Degree Health and Rehabilitation Sciences (Health and Aging) University of Western Ontario, London, ON, Canada
2004-2006	Master of Science Degree Kinesiology (Gerokinesiology) California State University Fullerton, Fullerton, CA, USA
1999-2003	Bachelor of Science Degree Physical Education and Sports Sciences Aristotle University of Thessaloniki, Thessaloniki, Greece

EXPERIENCE

2009	Research Assistant "Voices of youth through images of aging" University of Western Ontario
2007-2008	Research Assistant "An examination of exercise-related injuries in a sample of older adults attending a community-based older adults fitness facility" McMaster University
2006-2010	Editorial Assistant Journal of Aging and Physical Activity
2006-2009	Teaching Assistant Health Sciences University of Western Ontario
2006	Research Assistant "Frailty across the Health Care Continuum throughout Ontario" University of Western Ontario"

2006	Research Assistant "Effects of topical 024 essential oils on level of exercise during a 12-week exercise program for women with fibromyalgia: A randomized, placebo controlled study." California State University Fullerton
2006	Fitness instructor for people with Fibromyalgia California State University Fullerton
2006	Graduate Assistant Fitness Assessments Lab California State University Fullerton
2005-2006	Teaching Associate/Lecturer Kinesiology California State University Fullerton
2005-2006	Research assistant "Fall prevention center of Excellence Grant" California State University Fullerton
2005-2006	Research assistant "Walking Safe: Balance and Gait Assessment for Diabetic Patients" California State University Fullerton
2005	Technician in the Balance and Mobility program Center of Successful Aging
2005	Technician in the Senior Fitness Program Center of Successful Aging

RESEARCH AWARDS AND DISTINCTIONS

2008-2010	Graduate Research Thesis Award University of Western Ontario $3,500

2008-2010	Faculty of Health Sciences Graduate Student Conference Travel Award University of Western Ontario $1,400
2008-2009	Graduate Student Teaching Assistant Award (Nomination) University of Western Ontario
2008	National Initiative for the Care of the Elderly Travel Subsidy $1000
2007-2010	Health and Rehabilitation Sciences Program Conference Travel Award University of Western Ontario $1,400
2007	Travel Subsidy from the Society of Graduate Studies University of Western Ontario $150
2006-2010	Graduate Tuition Scholarship University of Western Ontario
2006	Kinesiology Graduate Research Presentation Award California State University Fullerton $200
2006	Fleckles Fund Student Travel Funding California State University Fullerton $500
2005-2006	Kinesiology Scholarship Award California State University Fullerton $600
2005	Alumni Association Scholarship for College of Health and Human Development California State University Fullerton $1,000

2005	Emeriti Memorial Scholarship California State University Fullerton $600
2000-2003	Greek State's Scholarship Foundation $6,800

MEMBERSHIPS

2010-Present	International Association of Gerontechnology
2010-Present	British Columbia Network for Aging Research
2009-Present	Canadian Dementia Knowledge Translation Network
2009-Present	Canadian Society for Exercise Physiology
2009-Present	Canadian Association on Gerontology
2008-Present	National Initiative for the Care of the Elderly
2006-2010	American College of Sports Medicine

CREDENTIALS

2006	Fallproof Balance and Mobility Specialist Instructor

RESEARCH TRAINING/SKILL DEVELOMENT WORKSHOPS

2010	Master Class International Association of Gerontechnology, Vancouver, BC
2009	Training to calculate frailty index using the deficits accumulation model Geriatric Medicine Research Center for Health Care of the Elderly Dalhousie University, Halifax, NS

2009 Summer Program in Aging
Canadian Institute of Health Research-Institute of Aging
Halifax, Nova Scotia

2008 NVivo Training Workshop
University of Western Ontario
London, ON

2008 Methodological Challenges in Health Research
University of Waterloo
Waterloo, ON

2007 Frailty: From concept to research to practice
Canadian Institute of Health Research-Institute of Aging
Calgary, AB

PEER-REVIEW JOURNAL PUBLISHED AND ACCEPTED ARTICLES

Theou O., Jones G., Overend T., Kloseck M., Vandervoort A. (2008). An Exploration of the Association Between Frailty and Muscle Fatigue. Applied Physiology Nutrition and Metabolism, 33(4), 651-665.

Theou O., Jones G., Brown L. (2008). The Effect of Rest-Interval on Recovery between Resistance Exercise Sets in Young and Old Women. Journal of Strength and Conditioning Research, 22(6), 1876-1881.

Theou O., Kloseck M. (2007). Tools to Identify Community-Dwelling Older Adults in Different Stages of Frailty. Physical and Occupational Therapy in Geriatrics Journal, 26(3):1-21.

Theou O., Jakobi J., Vandervoort A., Jones G. (accepted 2010). Daily Muscle Activity and Quiescence in Non-frail, Pre-frail, and Frail Older Women. Experimental Gerontology

PEER-REVIEW JOURNAL SUBMITTED ARTICLES

Theou O., Jones G., Jakobi J., Mitnitski A., Vandervoort A., (submitted April 2010). Relationship between Frailty and Physical Function Performance-based Measures. Journal of the American Geriatrics Society

Theou O., Stathokostas L., Roland K., Jakobi J., Patterson C., Vandervoort A., Jones G. (submitted November 2009). The effectiveness of Exercise Interventions for the Management of Frailty: A Systematic Review. Canadian Journal Aging

NON PEER-REVIEW JOURNAL PUBLISHED ARTICLES

Theou O. (2009). Frailty: A growing Area of New Research. "Age in Motion" Canadian Physiotherapy Association-Seniors Health division newsletter, 80:4.

PUBLISHED ABSTRACT

Theou O., Jakobi, J., Vandervoort, A., Jones G. (2009). Daily low threshold EMG in non-frail, pre-frail, and frail older women. Applied Physiology, Nutrition and Metabolism, 34 (S1):S93.

Theou O., Jones G., Jakobi, J., Vandervoort, A. (2009). Differences in Muscle Activity between Nonfrail and Prefrail Older Women during Daily Life. The Journal of Nutrition, Health & Aging, 13 (S1):S265.

Theou O., Jones G., Jakobi, J., Vandervoort, A. (2009). Using measures of fatigue to discriminate between levels of self-reported functional ability. Medicine and Science in Sports and Exercise, 41(5):S370.

Theou O., Hernandez D., Rose D. (2008). An Investigation of the Discriminative Validity of the 30 Foot-Walk test as a Function of Age and Gender. Journal of Aging and Physical Activity, 16 (S1):S197.

Theou O., Rose D., Hernandez D. (2008). An Investigation of the Discriminative Validity of the 30 Foot-Walk test as a Function of Age and Physical Activity Level. Journal of Aging and Physical Activity, 16 (S1):S208.

Hernandez D., **Theou O.,** Rose D. (2008). Can Gait Velocity Predict Which Older Adults Will or Will not Fall? Journal of Aging and Physical Activity, 16 (S1):S209.

Stathokostas L., **Theou O.,** Vandervoort A., Fitzgerald C., Belfry S., Lebrun C., Raina P. (2008). Psychometric Properties of a Questionnaire to Assess Exercise-Related Musculoskeletal Injuries in Older Adults. Journal of Aging and Physical Activity, 16 (S1):S34.

Theou O., Stathokostas L., Tran A., Jones G., Kloseck M., Vandervoort, A. (2008). Systematic Review on Exercise and Frailty. 37th annual scientific and educational meeting, Canadian Association on Gerontology (CAG), London, ON, Canada. The Canadian Association on Gerontology Conference Proceedings

Zecevic A., Magalhaes L., Culion C., **Theou O.,** Vlachos S., Leitch K. (2008). Acting Old: Learning About Aging Through Simulation and Photovoice. 37th annual scientific and educational meeting, Canadian Association on Gerontology (CAG), London, ON, Canada. The Canadian Association on Gerontology Conference Proceedings.

Theou O., Jones G., Vandervoort, A., Brown L. (2007). Effect of Rest-Interval on Decline of Power Between Sets of an Isokinetic Knee Extensor/Flexor Exercise in Old Women. Applied Physiology, Nutrition and Metabolism, 32 (S1):S86.

Theou O., Jones G., Brown L., Vandervoort, A. (2007). Effect of Rest-Interval on Decline of Torque Between Sets of a Isokinetic Knee Extensor Exercise in Young and Old Women. Medicine and Science in Sports and Exercise, 39(5):S299.

Theou O., French J., Hernandez D., Rose D., Jones J. (2006). Measuring Older Adult Gait Speed in Community Settings using the 30 Foot-Walk at Preferred and Maximum Speed. Medicine and Science in Sports and Exercise, 38(5):S331.

Jones C. J., **Theou O.,** Rutledge D., Lindemann J., Just N. (2006). Stability of Functional Fitness and Balance Performance Measures for Women with Fibromyalgia. National Fibromyalgia Association (NFA), National Fibromyalgia Continuing Medical Education Conference, Orange County, CA, USA. National Fibromyalgia Association Conference Proceedings.

Zafeiridis A., **Theou O.,** Manou V., Billis E., Dalamitros A., Kellis S. (2004). Fatigue during High Intensity Intermittent "Anaerobic" Exercise in Preteen, Teen, and Adult Females. Book of Abstracts of the 9th Annual Congress of the European College of Sport Science in Clermont-Ferrand, France.

Dalamitros A., Zafeiridis A., Dipla K., **Theou O.,** Manou V., Kellis S. (2004). Fatigue during Repetitive Maximal Knee Extensions in Boys, Teens, and Men. Book of Abstracts of the 9th Annual Congress of the European College of Sport Science in Clermont-Ferrand, France.

Billis E., **Theou O.**, Zafeiridis A., Manou V., Kellis S. (2003). Fatigue during Short-term Anaerobic Exercise in Pre-pubertal, Pubertal and Adult Females. 11th International Congress on Physical Education and Sports, Komotini, Greece. Exercise & Society: Journal of Sports Science.

Theou O., Billis E., Zafeiridis A., Manou V., Kellis S. (2003). Fatigue during Short-term Anaeorobic Exercise in Pre-pubertal, Pubertal and Adult Males. 11th International Congress on Physical Education and Sports, Komotini, Greece. Exercise & Society: Journal of Sports Science.

Theou O., Billis E., Manou V., Zafeiridis A., Kellis S. (2003). The Effects of Gender and Recovery Time on Fatigue during Short Term Anaerobic Exercise in Pre-pubertal and Pubertal. 11th International Congress on Physical Education and Sports, Komotini, Greece. Exercise & Society: Journal of Sports Science.

PRESENTATIONS AS A GUEST SPEAKER

Theou O. (2009). Aging and the Musculoskeletal System. Health Issues in Aging Undergraduate Course, University of Western Ontario, London, Ontario, Canada

Theou O., Jones G., Paterson D., Rice C., Vandervoort, A. (2008). Canada's Contribution to Aging and Physical Activity Research. 7th World Congress on Aging and Physical Activity, Tsukuba, Japan (Keynote invited Speaker).

Theou O. (2008). Frailty. Health Issues in Aging Undergraduate Course, University of Western Ontario, London, Ontario, Canada

Theou O. (2007). Exercise and Physical Activity for Older Adults. Invited speaker at 55 plus Senior's Group, Greek Community Center, London, Ontario, Canada

Theou O. (2007). Exercise in Middle Age. Invited speaker at the Daughters of Penelope group, Greek Community Center, London, Ontario, Canada