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EXAMINING THE ASSOCIATION BETWEEN MUSCULAR FATIGUE INDEX AND PHYSICAL FUNCTION IN MIDDLE-AGED WOMEN

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EXAMINING THE ASSOCIATION BETWEEN
MUSCULAR FATIGUE INDEX AND PHYSICAL
FUNCTION IN MIDDLE-AGED WOMEN

BY

OLIVIA FINNEGAN

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE
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MASTER OF SCIENCE THESIS

OF

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ABSTRACT

Importance and Objective: Rates of physical function (PF) limitations have increased over time in middle-aged (40-64 years old) women, however the pathway to functional decline has not been fully elucidated. The aim of this study was to examine the independent contribution of muscle fatigue to physical function performance, when compared to other known contributors to PF performance.

Methods: In this cross-sectional study, 104 middle-aged women (52.93 ± 6.10 years; BMI = 26.38 ± 5.10) were assessed in their performance of a 25-repetition fatiguing task in knee flexion and extension at 180 degrees per second and muscular fatigue index (MFI) was calculated as peak torque decline from the first three repetitions to the last three repetitions. Physical function was measured objectively through six assessments (transfer task, 30 second chair stand, 6-minute walk test, 8 foot up and go, lift and carry and lower-extremity physical function composite score). Physical activity was measured using accelerometry and physical activity logs. Whole body and regional composition were measured using Dual Energy X-ray Absorptiometry. Muscle strength was assessed using isokinetic dynamometry for isometric knee flexion and extension at 60 degrees, isokinetic knee flexion and extension at 60 degrees per second and 180 degrees per second, and muscle quality (MQ) was calculated as muscle strength normalized for thigh lean mass.

Discussion: When controlling for age, percent body fat, muscle quality and moderate to vigorous physical activity (MVPA) per day, MFI was only significantly associated with transfer task performance ($r=.260, p<0.05$), and higher MFI was associated with slower transfer task time. While MFI contributed to 3.5% of the variance in transfer

task performance ($p=0.024$), percent body fat contributed to 19.4% of the variance ($p=0.001$). Percent body fat was most highly related to all measures of physical function.

Conclusion: The strength of the association between MFI and physical function task performance decreased when other independent variables (percent body fat, MVPA, MQ) are taken into account. Therefore, muscle fatigue may be a less important target for intervention in this population, when compared to other stronger contributors to physical function.

Key Words: Middle-age, Physical function, Muscle fatigue index, Muscle quality, Body composition, Physical activity

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PREFACE

This thesis was written to comply with the University of Rhode Island Graduate School manuscript format. This manuscript “*Examining the association between muscular fatigue index and physical function in middle-aged women*” has been written in a form formatted for publication in *Menopause*.

TABLE OF CONTENTS

ABSTRACT	ii
ACKNOWLEDGMENTS	iv
PREFACE.....	v
TABLE OF CONTENTS.....	vi
LIST OF TABLES	vii
LIST OF FIGURES	viii
LIST OF APPENDICES	ix
MANUSCRIPT.....	1
CHAPTER 1	2
INTRODUCTION	2
CHAPTER 2	7
REVIEW OF LITERATURE	7
CHAPTER 3	40
METHODOLOGY	40
CHAPTER 4	49
FINDINGS	49
CHAPTER 5	53
CONCLUSION.....	53
APPENDICES	68
BIBLIOGRAPHY	98

LIST OF TABLES

TABLE	PAGE
Table 1. Participant Characteristics.....	61
Table 2. Muscle Characteristics	62
Table 3. Pearson’s Correlations Between MFI, Age, %Fat, MVPA, PT-180, MQ-180 and objectively measured physical function performance	63
Table 4. Partial Correlations between MFI and physical function assessments, when controlling for age, % fat, MVPA per day and MQ-180	64
Table 5. Regression Analysis Summary for Variables Associated with Physical Function Performance	65

LIST OF FIGURES

FIGURE	PAGE
Figure 1. Comparing mean MFI (muscle fatigue index) by menopausal status.	67

LIST OF APPENDICES

APPENDIX	PAGE
APPENDIX A. Women’s Health Improvement Initiative screening questionnaire....	68
APPENDIX B. Women’s Health Improvement Initiative informed consent.....	88
APPENDIX C. Physical Activity Readiness Questionnaire (PAR-Q).....	93
APPENDIX D. Mini-Mental State Examination (MMSE).....	94
APPENDIX E. Actigraph Accelerometer Instructions	96
APPENDIX F. Actigraph Accelerometer Record of Wear.....	97

MANUSCRIPT

Examining the Association Between Muscular Fatigue Index and Physical Function in Middle-Aged Women

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CHAPTER 1

INTRODUCTION

Physical function performance, the ability to perform the basic activities associated with maintaining independence, is a growing concern in the middle-aged population (1). Rates of physical disability and physical function limitations have increased substantially in middle-aged populations, with a higher increase noted in women (2). Physical function limitations are associated with increased risk of falling, loss of independence and lower quality of life with advancing age (3). This trend in middle-aged women is of particular concern due to the recent research that has identified health status at midlife as an independent and significant determinant of health at older age (4)(5)(6). With our rapidly aging society (7), this raises concerns on how to appropriately intervene in an effort to improve health outcomes and promote healthy aging among women in their transition to older adulthood.

Reducing the risk of functional decline across the lifespan is related to preventing physical disability in older age (2). The midlife period in women has been identified as a critical timeframe for the onset of physical function limitations, when targeted prevention strategies could greatly reduce the risk of declining physical function with age (2)(8). Engaging in physical activity during middle-age years can improve health-related outcomes in older age by preventing the loss of muscle mass and improving cardiorespiratory fitness (4). Research also has indicated that the physical disability pathway and initiation of physical function limitations in midlife is

more of a dynamic process and can be reversed (9), whereas the prognosis is typically poorer in older adults (10) demonstrating the malleable nature of the midlife period for effective intervention.

While the pathway to functional decline has been more fully elucidated in older populations (11), research is needed to identify the most salient factors determining physical function deficits in middle-age. The manifestation of functional decline in middle-aged populations may be more subtle than the changes seen in older adults (12), such that there are preclinical signs appearing before overt mobility limitations. Preclinical signs that may appear in the middle-aged population include a reduced walking pace, rest at intervals, or use of a walking aid (13). The use of compensatory strategies, like using the arms of the chair to assist with standing up, or modifying the physical task, for example reducing the pace of the task, may indicate physical function decline in midlife, whereas self-reported difficulty performing in physical functional tasks is typically more indicative of physical function decline in older adults (12).

Currently available research indicates that in middle-age declines in physical activity exacerbate a shift in body composition, in which fat-free mass decreases and body fat percentage increases (14)(15). Additionally, muscle quality, defined as muscle strength normalized for lean mass, is independently associated with poorer physical function in middle-aged women (14), highlighting the importance of both lean mass and muscular capacity for optimal functional performance. The culmination of these age-related changes can lead to functional decline in middle-aged populations.

However, it is unclear to what capacity muscle fatigue, a valuable parameter of muscle function, modulates this decline.

Muscle fatigue, defined as a decrease in the ability of a muscle to generate force, has been shown to be increased to a greater extent in older populations (>65 years old) during high-velocity dynamic contractions when compared to younger people (16)(17)(18). This task-specific increase in fatigability has implications for physical function (19)(20) as older women with a history of falling demonstrate greater muscle fatigue compared to older women with no history of falling, independent of muscle strength (21). Muscle fatigue is a valuable variable to assess in association with physical function, as muscle fatigue during power-based contractions can be representative of the decline in physical performance in older adults throughout the day (22). Older adults are often working at their maximal capacity or utilizing compensatory strategies (23) when completing activities of daily living (ADLs), (24). Since age is associated with an increase in the level of effort required to perform ADLs (24), any reduction in the ability to generate force during a task could worsen their performance of the ADLs.

The etiology of muscle fatigue as it relates to physical function is not well elucidated, although there are various possible mechanisms. Increased muscular fatigue associated with aging could be due, in part, to the increased energetic cost of muscular contractions (25). There has been a demonstrated age-related increase in the coactivation of agonist and antagonist muscle groups during a muscular contraction (25), which has been identified as a compensatory strategy to improve stability during tasks (26). Coactivating the antagonist muscle group (hamstrings) with the

contraction of the agonist muscle group (quadriceps) during knee extension is a typical motor control strategy that improves joint stability and movement accuracy (27). However, the coactivation of antagonist muscles is disproportionately increased in muscular contractions performed by older adults (25), and increases the energetic cost of work for older populations. Concerningly, this increased coactivation with muscular contractions has been implicated in declines in physical function and mobility in older adults (65-90 years old) (24)(28), indicating the unique role that muscle fatigue may play in physical function.

Women in particular are under-represented in exercise science research, and even more substantially in muscle fatigue research (29). Physical function deficits are becoming more apparent and increasing temporally in middle-aged women (2), with a prevalence of 20% to 40% (30). Middle age is a critical period for women, with the onset of menopause and the subsequent physiological changes associated with this transition. The hormonal changes associated with menopause can further exacerbate the age-related decline in muscle mass (31), muscle strength (32)(33), and muscle quality (34), contributing to the vulnerability of this population. Additionally, during midlife, physical activity levels decrease due to socio-behavioral aspects and changes in lifestyle, in which physical activity levels decline due to access to fitness facilities and perceived barriers to exercising, such as time (35). Age-related declines in physical activity and body composition changes also have been identified as factors in physical function decline in middle-aged women (14). It has been demonstrated that muscle fatigue can contribute to functional decline in older populations (19), however it is unclear whether muscle fatigue has an influence on physical function in this

population. Understanding the association between muscular fatigue and physical function in middle-aged women would allow researchers to determine the merit of using muscle fatigue as a targeted measure in intervention studies with middle-aged women experiencing functional decline. Muscle fatigue could be targeted through a muscle endurance-based resistance training program emphasizing lighter loads, higher repetitions and shorter rest intervals (36), which would be different than an intervention emphasizing muscle strength that utilizes higher loads, lower repetitions and longer rest intervals.

Therefore, the primary aim of this study was to assess the strength of the association between muscle fatigue and objectively measured physical function performance in middle-aged women. We hypothesized that women with higher MFIs, indicating better fatigue resistance, will have better physical function performance on five objectively measured physical function tasks, when controlling for age, body composition and physical activity level.

CHAPTER 2

REVIEW OF LITERATURE

Introduction

Physical disability is increasingly impacting middle-aged populations (2). Middle-aged women, in particular, are more susceptible than men to functional limitations and physical disability associated with increasing age, with 20 to 40% of midlife women reporting physical function limitations (8). Physical disability and inadequate physical function are of concern as they are related to loss of independence and lowered quality of life (37). While increased prevalence of disability and decreased physical function in middle-aged women is concerning, research indicates that middle age may be a critical time to intervene to improve physical function performance and related health outcomes. Health status during middle-age is predictive of health outcomes later in life (38) and the transition from middle-age to older adulthood is highly influenced by a number of risk factors in midlife. However, the disability pathway in middle-aged women is a dynamic process, such that targeted and appropriate intervention may be able to aid in reversing physical function decline (8)(9).

As the US is experiencing a rapid demographic transition due to population aging (7), it is imperative to examine health at midlife to optimize healthy aging outcomes. It is estimated that between 2000 and 2050, the number of older adults (>65 years old) in the United States will increase by 135%, indicating that a large

number of middle-aged individuals are transitioning to older adulthood over the next several decades (7). These individuals are entering older adulthood with multiple chronic conditions and comorbidities (39). Mortality for older adults has declined and older adults can live longer with chronic conditions than previously (40), therefore, while there is a growing number of older adults, older age is met with poorer health.

It is imperative that we have a comprehensive understanding of successful aging across the lifespan. Successful aging is comprised of survival, lack of disability, life satisfaction, social engagement, productivity, quality of life, and the absence of disease (41). There is a two-factor model utilized to assess successful aging based on both objective and subjective components (42). The objective component of successful aging includes having few chronic diseases, high functional ability and little to no pain. The subjective component of successful aging is the self-evaluation of aging and how the individual feels about their aging experience. Since it has been established that health status during midlife is a determinant of health outcomes in older adulthood (43)(44)(4), middle-age is a critical time for targeted interventions designed to promote successful aging across our rapidly aging society.

Successful aging is dependent, in part, upon one's physical function ability, which is defined as the ability to perform basic activities associated with maintaining independence (1). Physical performance limitations are predictive of physical disability, increased health care usage, loss of independence, and increased risk of mortality, indicating that physical function is independently associated with poorer health outcomes (45). The decline in performance of activities of daily living (ADLs) in older adults is dependent on the interaction of various physical, psychological,

social, and environmental influences (46)(3). Typically, as we age, there is an increasing metabolic cost required to perform ADLs (24). To maintain their independence, some older adults use compensatory strategies to complete ADLs (23), such as the modifying of the way in which an activity is performed, and the use of these strategies is independently associated with adverse health outcomes (47). Once functional decline and physical disability is apparent in older adults, especially women, the prognosis for health-related outcomes is poor, as the majority will continue to experience worsened physical function as they age (10). While this pattern of functional decline leading to physical disability has been observed regularly in older women, the nature of this association is not as well characterized among middle-aged women. It appears that functional limitations are more dynamic during midlife, in that declines in physical function can be improved or adequate physical function can be maintained (9). Therefore, adopting health behaviors associated with improvement or maintenance of physical function during midlife may be critical to reversing functional decline and improving health outcomes as this population enters older age, but currently, the literature examining physical function in middle-age is limited.

Our current understanding of the factors that are associated with optimal physical function is shaped primarily from studies of older adults (11), as there is a wealth of literature examining the most salient contributors to physical function in this population. Research has identified age, physical activity levels, body composition, muscular strength and endurance, muscle quality, and muscle fatigue as independent factors associated with physical function performance in older adults. The limited

information examining the factors associated with physical function performance in middle-aged women also show that age, physical activity levels, body composition, muscular strength and endurance, and muscle quality are independently associated with physical functional ability (14). However, research assessing how muscle fatigue influences functional performance is limited, and most studies examining physical function and muscle characteristics have focused on muscle mass, strength and power. The lack of clear standardization of the methods in measuring muscle fatigue may be contributing to the shortage of research examining this association.

The following review of literature will examine muscular fatigue and its potential influence on physical function performance in middle-aged and older adults. The review will also discuss the associations between physical function and other more well-established independent contributors including, age, physical activity level, body composition, muscle strength, and muscle quality. Understanding the strength of the association between muscle fatigue and physical function, and how this compares to other known contributors, will allow researchers to identify potential targets for intervention when designing exercise programs focused on maintaining and improving physical function in middle-aged women, in hopes of reducing physical disability and functional decline with increasing age.

Physical Function Performance in Middle-Age

Physical function is characterized by one's ability to perform basic tasks involved with living independently (1). These activities of daily living involve components of cardiovascular fitness, muscular strength and endurance and balance

(1). Physical function limitations have demonstrated implications for physical health, mental health, risk of falls and bone fracture, quality of life, and healthcare costs (3). While physical function ability and its determinants have been extensively examined in older populations, less has been done with samples of middle-aged adults. Additionally, recent findings from the Study of Women's Health Across the Nation (SWAN) indicate that limitations in physical function are present for a large number of middle-aged women; 20% of women aged 40 to 55 had self-report limitations in physical function and the prevalence of physical function limitation increased in women ages 56-66 to 55% (48).

The growing prevalence of physical function limitations among middle-aged adults is concerning as it is associated with negative implications for various health outcomes later in life (49). Wolinsky et al. (47) longitudinally studied self-reported subclinical status, or preclinical disability, and its impact on adverse health outcomes in nine hundred ninety-eight African-American men and women ages 49-65, with a follow-up of three years. Subclinical status, or preclinical disability, is an approach used in evaluating the pathway of functional decline and this status can be thought of as an intermediary step in the disablement process before the onset of perceived task difficulty for the individual. Using subclinical status can identify those who are at risk for developing physical function limitations, who may have gone unnoticed when assessing with the traditional approach which only evaluated task difficulty. Subclinical status was assessed at baseline by examining lower body function, activities of daily living (ADL) and instrumental activities of daily living (IADL). Adverse outcomes were evaluated for the three years following baseline, and included

lower body limitations, difficulty with ADLs and IADLs, physical performance on the Short Physical Performance Battery (SPPB), physician visits, hospitalization, nursing home placement and mortality. It was found that subclinical status for functional limitations at baseline was predictive of lower-body functional limitations, ADLs, IADLs, number of physician visits and hospitalization at follow up. This work demonstrates that compromised physical function in middle-age is predictive of worsened health outcomes as one ages. The pathway to physical disability and disablement can be viewed as a process, and as these conditions depend partially on one's ability to have adequate physical function, it is imperative that we understand the factors that contribute to physical function across the lifespan. As there is significant lack of literature addressing physical function performance in middle-age, this highlights the need for additional research in this area.

Muscle Fatigue: Definition, Measurement and Associations with Age, Sex, and Physical Function

Muscular fatigue is defined as the decline in the ability of a muscle to generate force (50). Skeletal muscle fatigue is characterized by a decline in performance characterized by a reduction in force generated with repeated muscular contraction that can be reversed with recovery (51). Muscle fatigue has both central and peripheral components. Peripheral fatigue is the reduced ability of the muscle cells to produce energy metabolically, while central fatigue originates from the central nervous system and decreases neural drive to the muscle (52). It has been suggested fatigability is driven primarily by peripheral fatigue, with estimates that 80% of the

fatigue responses is due to peripheral factors. (53). This demonstrates that the majority of force decline with repeated muscular contraction is related to metabolic components, rather than neural drive (54). Specifically, the primary driver of peripheral fatigue is the accumulation of inorganic phosphate (Pi)(55), resulting from the rapid breakdown of creatine phosphate. In addition to accumulated Pi, the anaerobic breakdown of glycogen during glycolysis also leads to increased levels of H^+ , as it rapidly dissociates from lactic acid, thus decreasing the pH level of the blood, hindering enzyme activity and contributing to the onset of fatigue (56). It was previously thought that lactic acid accumulation was the cause of skeletal muscle fatigue, however, it is now understood that excess Pi decreases maximal cross-bridge force, causing a decline in force generation, thus contributing to muscle fatigue (56).

Research has indicated that muscle fatigue is independently related to physical function. There is an age-associated increase in muscular fatigue (17), which has been independently associated with a decline in physical function (19)(28), particularly during fast dynamic muscular contractions (16), that has been demonstrated in adults over 80 years old (57). Older adults experience an increased energetic cost of muscular contractions by the increased coactivation of agonist and antagonist muscles during muscular contractions (25). The increase in coactivation with contractions has also been associated with decreased physical function and mobility in older adults ages 65-90 years old (24)(28). Since there is an increase in the level of effort required to perform ADLs in older adults, any reduction in the ability to generate force can significantly impact physical function outcomes, indicating the importance of muscular fatigue as a parameter to assess physical function.

Measuring and Quantifying Muscle Fatigue

Muscle fatigue can be measured in several ways. One noninvasive measure of muscle fatigue is the Fatigue Index (58). This is a quantitative measure of muscle endurance that directly indicates the reduction in force-generating capacity of a muscle (58). The Fatigue Index can be calculated by determining the difference in average peak torque generated at the beginning of a fatiguing task and average peak torque generated at the end of a fatiguing task (i.e. difference in average peak torque from the first three repetitions and last three repetitions in a 25 repetition knee extension flexion task) (59). This is typically measured using isokinetic dynamometry, which is a laboratory measure that allows the working muscle to contract at a constant velocity (60).

While the Fatigue Index has widely been used for quantifying fatigue in various populations, the calculation used to derive Fatigue Index is variable across literature (58)(59)(61). Milner-Brown et al. (58) first tested the reproducibility and reliability of the methods in measuring and quantifying muscle fatigue. Fatigue Index was calculated as the initial maximum force minus maximal force after 60 second contraction divided by the initial maximum force and multiplied by 100. Fatigue Index was cited as a reliable measure to quantifying human muscle fatigue. Gentil et al. (59) also utilized the Fatigue Index and calculated FI as percent peak torque difference in the first and last three repetitions of the fatiguing protocol. The FI was used by Katsiaras et al. (61), measured as $(\text{final torque}/\text{initial torque}) \times 100$. Lastly, Silva et al. (62) examined muscular fatigue calculated using the Fatigue Index as percentage of work (W) decline through the test with the equation: $100 - (W \text{ latter } 1/3$

/ W former $1/3 \times 100$). While the calculation used to determine Fatigue Index is variable across literature, all of these calculations indicate the rate of torque decline over the course of a fatiguing task.

Muscle Fatigue and Aging

When assessing age-related changes in fatigue, the findings are highly dependent on both contraction type (isokinetic vs. isometric) and contraction velocity. Dynamic tasks have been associated with greater fatigue in older adults compared to isometric tasks, whereas isometric force losses are similar in younger (18-40 years old) (63) and older adults (>65 years old)(63), and in some instances, older adults have even been shown to be more fatigue resistant during isometric tasks compared to younger adults (22). Therefore, the preferred method of muscular capacity assessment, isokinetic testing, can measure torque across the entire range of motion of a joint during repetitive contractions, which has been shown to be a more integrated assessment of muscular endurance, strength, and fatigue in older adults (64). Isokinetic assessments may be more indicative of the functional capacity of muscle and identify those at risk for mobility impairments.

Contraction speed during isokinetic induced fatiguing tasks is also an important factor to consider when quantifying fatigue. An isokinetic fatiguing task of 100 repeated maximum knee extension contractions at 90 degrees per second resulted in no significant difference in Fatigue Index between younger and older participants (65). Dynamic fatiguing tasks at low (60 degrees/second) to intermediate contraction speeds (120-180 degrees/second) have also been shown to produce no significant difference in fatigability between younger and older adults (16)(66)(67). However,

older adults demonstrate increased fatigability during isokinetic fatigue testing at high contraction velocities (typically above 270 degrees/second), compared to younger adults (19)(68), specifically in the knee extensor muscles (19).

Baudry et al. (69)(2007) compared the neuromuscular fatigability of the ankle dorsiflexor muscles during five sets of thirty maximal concentric and eccentric contractions in young (22-47 years old) and old (72-87 years old) individuals. The mechanism underlying age-related fatigue was also investigated in this study using superimposed electrical stimulation, which evaluated the activation of the muscle during contraction, and they found greater fatigability of the ankle dorsiflexor muscles in older adults compared to younger. Muscle fatigue in both younger and older adults was associated with peripheral factors stemming from calcium-controlled excitation-contraction coupling processes. However, only older adults experienced a change in M-wave amplitude and area with fatigue. A decline in M-wave amplitude in older adults, signifying a reduction in muscle action potential, indicates that fatigue in older adults may be attributable to reductions in peripheral excitation, or potentially, the insufficient propagation of the nerve potential. Contrastingly, Lanza et al. (70) assessed fatigue of the ankle dorsiflexor muscles during intermittent isometric and dynamic maximum voluntary contractions and discovered that there is greater fatigue resistance in older men (72 +/- 4 years) compared to younger men (26 +/- 4 years). This study also assessed both central activation, using electrical stimulation, and peripheral excitability, by evaluating the compound muscle action potential (CMAP). There was no observed central activation failure associated with fatigue in both the younger and older group. The compound muscle action potential (CMAP) was higher

in the younger men before exercise; however, fatigue did not impact CMAP amplitude from the fatiguing tasks in either group. There were no age-related alterations in central or peripheral activation that explained why older men in this study were more fatigue resistant. They postulated that greater fatigue resistance in older adults was related to factors in the muscle itself, such as age-related changes in muscle metabolism, in which older adults experience less accumulation of Pi and H⁺ protons, which both are inhibitory metabolites that play a role in muscle fatigue development. Baudry et al. (69) utilized a lower speed of movement (50 degrees per second rather than 90 degrees per second) compared to Lanza et al. (70) and the concentric and eccentric contractions began after an isometric maximal voluntary contraction (MVC), resulting in full activation of the involved muscles for the contraction and this may explain the discrepancy in findings between these two studies.

Limited research suggest that there may be an age-related increase in fatigability during maximal dynamic contractions (19)(69)(68). Increases in muscular fatigability with age occur as a result of neuromuscular factors, including neuromuscular fatigue (69) and decreased motor unit recruitment(71)(72); however, the mechanism for this decline may be related to metabolic capacity, as age is associated with decreased capacity for oxidative ATP synthesis, related to a decline in mitochondrial function with age (73).

Muscle Fatigue and Sex

There are a number of established sex differences that can impact one's resistance to fatigue (29) and these differences are specific to the fatiguing task. During isometric tasks, women are more resistant to fatigue at the same relative

intensity, or percentage of maximal strength, compared to men, despite men typically having greater absolute muscular strength compared to women (29). It is not well understood whether this fatigue resistance in women is the same for dynamic tasks, as there have been variable findings across the literature (74). The proposed mechanisms responsible for sex differences in muscle fatigue include contractile mechanisms, as there is a higher energy utilization in men than in women attributable to contractile speed, which reflects the reduced capacity for aerobic energy production in men when compared to women (75). Women are also underrepresented in fatigability research, possibly due to hormonal fluctuations and pregnancy, which further emphasizes the need for research focusing on muscle fatigue in this population.

Muscle Fatigue and Physical Activity

While the age-related decline in physical activity can contribute to muscle mass and strength loss associated with aging (76), there is inconclusive evidence on whether this same relationship exists for muscle fatigue. Examining fatigue during an isokinetic fatiguing task could show function across the entire functional range of motion during repetitive contractions and may provide more insight into one's functional capacity and be more sensitive in identifying physical function decline than only assessing muscle strength or mass (64). It has been established that regular physical activity improves muscle function and can reduce the susceptibility to muscle fatigue in individuals of all ages (77). Depending on the type of physical activity, there are various ways in which physical activity can enhance fatigue resistance, including an increase in enzymes that improve oxidative metabolism and an increase in muscle oxidative capacity (77). Endurance exercise training also increases VO₂, or

maximal unloaded shortening velocity, in type I muscle fibers, which can make them more fatigue-resistant (78). The impact of physical activity on muscle fatigue has been well-studied in younger athletic populations, however more research is needed focusing on these associations in middle-aged and older aged populations.

In 1990, LaForest et al. (79) explored the impact of an active lifestyle on muscle strength and muscle endurance, and fatigue, in eighty younger and older men and women. This study was comprised of the groups: young active men (30.4 +/- 3.3 years), young active women (27.5 +/- 4.3 years), elderly active men (64.4 +/- 3.7 years), elderly active women (65.3 +/- 4.5 years), young sedentary men (29.2 +/- 3.4 years), young sedentary women (25.6 +/- 4.4 years), elderly sedentary men (65.2 +/- 3.2 years), and elderly sedentary women (65.6 +/- 4.4 years). Muscle fatigue was measured with a cumulative fatigue index (FI) for a fifty-repetition task at 3.14 rad/s. FI in that study divided the sum of the peak torque from the last twenty-five contractions by the sum of the peak torque from the first twenty-five contractions in a fifty-repetition task at 3.14 rad/s. No age-related difference in fatigability were found, however the active group, across both genders and age groups, was significantly more resistant to fatigue than the sedentary group (p -value < 0.05).

A 2011 meta-analysis by Avin and Law (80) looked at the variation of age-related differences in muscle fatigue by contraction type (isometric vs. isokinetic), and assessed physical activity in its association as a moderating variable to muscle fatigue. Physical activity level was not significantly related to muscle fatigue, across all contraction-type subgroups. However, physical activity was assessed as either being

active or sedentary, with no indication of volume of activity, which can limit the scope of assessing the continuum of physical activity levels.

It is plausible to expect that physical activity levels would play a role in the development of task-specific muscle fatigue, which can further depreciate physical function loss with age. However, based on the current literature, there is still no clear association between physical activity and muscle fatigue. Current literature is limited by smaller sample sizes and binary assessments of physical activity. It has already been established that decreased physical activity levels with age can contribute to the onset of muscle mass and strength loss, particularly in women (14).

Muscle Fatigue and Physical Function

When specifically examining muscular fatigue in laboratory based conditions using isometric dynamometry, task-specific increases in fatigue with age have been shown, such that older adults experience greater fatigue, or loss of muscular production capability, during high-velocity dynamic contractions, compared to younger adults (17)(16)(18). If aging is associated with a more significant loss in the ability to maintain force output, as demonstrated by increasing muscle fatigue, muscular fatigue may be an important factor to measure when examining the independent factors associated with one's ability to complete activities of daily living with undue stress.

Independent of losses in muscle strength and quality, muscle fatigue has been linked to physical function deficits of older age (over age 65) (21). However, it is important to note that the current literature examining the associations between muscle fatigue and physical function in older adults has mixed findings due to the high

variation in physical function assessments used among studies. Additionally, fall risk and physical function are highly related, as physical function performance is an independent predictor of one's risk of falling (81). Due to the interrelationship between physical function and fall risk, for the purpose of this literature review, fall risk will be included under the domain of physical function.

A 1997 study by Schwendner et al. (21) examined age differences in fatigability in women with and without a history of falling. Twenty-nine young women (mean age of 21.6 years old), twenty-six older women with a history of falls (>65 years old), and twenty-seven older women with no history of falls (>65 years old) completed repeated concentric contractions of the quadriceps using isokinetic dynamometry at a contractile speed of 60 degrees per second until force output was below 50% maximum voluntary contraction (MVC) for two consecutive repetitions. Older women with a history of falls were faster to fatigue during the task, compared to the other groups (both $p < 0.05$). Interestingly, muscular strength, measured by MVC, was not significantly different between the women with a history of falls and women with no history of falls, suggesting that muscular fatigue may play an independent role in fall risk.

The relationship between fatigability and physical function in older adults was further elucidated in a study published in 2014 (28). Fatigability was assessed by submaximal isometric contraction of the dorsiflexor muscles in which participants had to maintain a foot position while supporting a load of 20% one repetition maximum. Mobility was measured via a sit-to-stand task and time to walk 500 meters. Older adults (65-90 years old) demonstrated increased fatigue in comparison to young adults

(19-30 years old) and fatigability of the dorsiflexors was significantly correlated with motor function. Coactivation, a valuable motor control strategy where agonist and antagonist muscles surrounding a joint contract simultaneously (82), was also found to be associated with various components of motor function, including sit-to-stand time ($p<0.05$), strength ($p<0.05$) and steadiness ($p<0.05$) only in older adults. Increased coactivation with age has been posited as a compensatory strategy that older adults use to provide joint stability during ADLs (26). This presents a possible mechanism for the unique role that muscle fatigue may play in determining physical function outcomes, as increasing muscle coactivation of agonist and antagonist muscles during a contraction can increase the energetic cost of work (25), thus resulting in more difficulty completing activities of daily living.

Kent-Braun et al. (67) assessed muscle weakness, fatigue and torque variability in relation to mobility status, using the Short Physical Performance Battery (SPPB) in young and old women. Eight young healthy women, nine older healthy women and eight older women with mild to moderate mobility impairments underwent assessment of muscle fatigue using a four-minute protocol of maximal dynamic contractions at 120 degrees per second, an intermediate velocity, and was quantified with the equation: $100 \times (\text{average of final 5 contractions}) / (\text{average of peak dynamic torque at baseline and peak torque achieved through the fatigue protocol})$. Fatigue was not significantly different across the three groups; however peak torque was higher in the younger group compared to both older groups (both $p<0.001$) and peak torque was higher in the older healthy group compared to the older group with mobility impairments ($p<0.001$). Torque variability was significantly greater in the older

impaired group, compared to the younger group. Mobility status and muscular fatigue resulting from an intermediate-velocity dynamic fatiguing task were not significantly associated; however, the findings support the idea that muscle weakness and muscle fatigue are independent of one another in their role in muscle function. While this novel finding contributes to the small amount of literature in this area, the small sample size of this study ($n=25$) limits the generalizability of this study.

Senefeld et al. (19) examined age-related fatigability during high-velocity dynamic contractions of the elbow flexor and knee extensor muscles in relation to functional performance (balance and walking endurance) in thirty-five young (18-31 years) and thirty-two older (60-85 years) healthy men and women. Participants performed three sets of thirty maximum voluntary concentric contractions (MVCC), with each set followed by one maximum voluntary isometric contraction (MVIC). The physical function performance of only the older adults was assessed through a balance assessment and the 6-Minute-Walk-Test (6MWT), which were both evaluated in the introductory session. Self-report physical activity was also collected from both younger and older adults. The knee extensor muscles were more impacted by age-related increases in fatigability than the elbow flexor muscles ($p=0.014$). Higher fatigability of the knee extensor muscles was associated with poorer physical function in older adults as indicated by less walking endurance and depressed balance, in addition to lower physical activity levels. This same effect on physical function was not found in the elbow flexor muscles. The loss of ability to perform tasks with the lower body is more highly related to physical function and performance of ADLs for

older adults (83), which makes evaluating age-related changes in muscles of the lower body most important in its association to mobility and functional decline.

Contrastingly, Roshanravan et al. (64)(2016) examined isokinetic work and fatigue and their associations to persistent severe lower extremity limitation (PSLL) and all-cause mortality in 71-82-year-old adults. The Fatigue Index, measured using 30 maximal knee extensions at 180 degrees per second, was not associated with PSLL or all-cause mortality. Both Senefeld et al. (2017) and Roshanravan et al. (2016) examined the associations between knee extensor muscle fatigue and functional performance, however methodological differences may be responsible for their conflicting findings. PSLL was measured subjectively and defined as two consecutive reports of having difficulty or being unable to walk a quarter of a mile or climb ten steps without resting, which was evaluated at all 6-month follow-up visits, while Senefeld et al. (19) used the Berg Balance and six-minute walk test to measure physical function. Roshanravan et al. (64) used a binary approach (classified as either presence or no presence of PSLL) to assess functional performance and may underestimate the presence of functional limitations, as functional performance is often viewed as a process or a continuum. The way each study evaluated physical function also targeted different characteristics of physical function, which may have impacted the results. The presence of PSLLs indicated the loss of cardiorespiratory endurance, while Senefeld et al.'s study (19) investigated balance, in addition to cardiorespiratory endurance and muscular endurance during the 6MWT. Furthermore, the methods of these study were vastly different in their fatiguing tasks. The Senefeld et al. (19) protocol elicited more fatigue in the protocol with three sets of thirty

MVCCs with each set of MVCCs followed by one MVIC, while the Roshanravan et al. (64) study had a fatiguing task of thirty maximal knee extensions at 180 degrees per second.

The variations in the methods used to assess both muscle fatigue and physical function across studies limits the ability to draw conclusions about the independent role that muscle fatigue plays in determining physical function. When evaluating these associations, it is also important to consider the specificity of the fatiguing protocol (contraction type and velocity), in that it should appropriately simulate the type of fatigue that would theoretically occur during completion of ADLs. As natural gait can produce knee angular velocities over 350 degrees/second while walking and 140 degrees/second when standing from a chair (84), this highlights the importance of testing at intermediate to higher contraction velocities. There is further research needed to establish the optimal method for assessing muscular fatigue when examining the association between muscular fatigue and physical function in different populations.

Other Established Factors Associated with Physical Function: Body Composition, Physical Activity, Muscle Strength, and Muscle Quality

Body Composition

Aging is associated with changes in body composition, specifically an increase in fat mass and decrease in lean muscle mass (85). The lean mass decline occurs more prominently in muscles of the lower body (86)(87), and this may have a significant impact on physical function ability, as the majority of ADLs require use of the lower

body. Women are at an increased risk for more dramatic decreases in muscle mass, due in part to hormonal changes associated with the menopause transition in midlife (88). Muscle mass begins to decrease after the third decade and begins to accelerate in its decline after the fifth decade of life in women (89). The accelerated decline after age 40 may be associated with hormonal changes resulting from the menopausal transition (90). Menopause, the cessation of menstrual periods with the loss of ovarian follicular activity, is associated with increased hormone instability (91) and these dramatic hormone changes are associated with increases in body fat, and declines in muscle mass (31). The decline in estrogen with menopause is associated with a loss in bone mineral density (BMD), an increase in visceral adiposity, an increase in the risk of metabolic disorders and a decline in quality of life (92). Loss of muscle mass with age is an independent predictor of falls and is associated with an increased risk of functional limitations and physical disability with age (93). The impact of aging on muscle mass loss can have modulatory influences from variables including smoking, sedentary lifestyle, poor health, height, weight and genetic influences (94).

Maltais et al. (88) identified various factors that contribute to muscle mass and strength loss in post-menopausal women. Sex hormones play an important role in the decline in muscle mass associated with menopause as estrogen and insulin like growth factor -1 (IGF-1), a hormone important in muscle protein synthesis that mediates the effect of pituitary growth hormone (95), both decline with menopause. Decreased estrogen is also associated with increases in oxidative stress, which is a contributing factor to sarcopenia (muscle mass loss associated with aging). Growth hormone (GH) also plays an important role in body composition regulation and declines with

menopause, further accelerating the loss of muscle mass and may play a role in increasing visceral fat. Additionally, menopause is associated with a decline in dehydroepiandrosterone, or DHEA, a prohormone that helps in the synthesis of sex hormones, which has been associated with reductions in muscle mass and worsened physical performance. These hormonal changes associated with menopause play an integral role in muscle mass loss in post-menopausal women.

A more recent longitudinal study further examined the association of the menopause transition and changes in body composition (90). One thousand two hundred and forty-six participants with a mean baseline age of 47.1 (SD, 2.6) years old participated. They found that increasing fat mass and decreasing lean muscle mass was evident prior to the menopause transition, from eight years to two years before the final menstrual period (FMP), however this shift in body composition accelerated through the menopause transition and stabilized in post-menopausal participants. Prior to the menopause transition, fat mass increased by 1.0% per year ($p<0.0001$), which then accelerated to 1.7% ($p<0.0001$) during the menopause transition, which was measured as two years before the FMP to one and a half years after the FMP. Before the menopause transition, there was a decrease in lean proportion mass by 0.2% per year ($p<0.0001$), while during the menopause transition, this was accelerated to a 0.6% decline in lean proportion mass per year ($p<0.0001$). This study primarily indicates that an unfavorable shift in body composition (loss of lean muscle mass, increase in fat mass) occurs in middle age and these changes are further exacerbated with the menopause transition.

Yamada et al. (96) examined age-dependent changes in skeletal muscle mass and the visceral fat area in a population of Japanese men and women ages 40 to 79 years old. In women from age 40 to 79, visceral fat area increased by 65.3% and the skeletal muscle mass index decreased by 6.4%. Visceral adiposity, fat distribution in the abdominal area, is hormonally active, meaning that it releases inflammatory cytokines which can contribute to the progression of metabolic syndrome and cardiovascular disease (97). This study suggested that the age-related increases in visceral adiposity, and the subsequent release of inflammatory cytokines from this metabolically active fat storage, may contribute to the loss of skeletal muscle mass. This is plausible as high levels of inflammatory markers, such as interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF- α) are associated with a greater decline in muscle mass over the course of five years, due to the catabolic impact of these markers on muscle (98). However, Yamada et al. (96) was cross-sectional in its assessment and the direction of this relationship cannot be determined by this association of high visceral adiposity and low muscle mass.

It is evident that there is an age-dependent change in body composition, in which muscle mass decreases and fat mass increases, and this is exacerbated in women, particularly during the menopause transition (90)(88). The hormonal changes associated with menopause, including declines in estrogen, IGF-1, GH and DHEA contribute to this shift in body composition (88). Lastly, visceral adiposity increases significantly in middle-aged women and the catabolic effect of the inflammatory markers released may contribute to more muscle mass loss with age (96).

Physical Function and Body Composition

These body composition changes associated with aging, particularly in women, have implications for physical function. The loss of muscle mass and increase in fat mass with age can contribute to decreases in physical function and vulnerability to falls and physical disability (93)(99). In middle-aged women, sarcopenic obesity, the presence of sarcopenia in obese individuals, is associated with worsened physical function outcomes, when compared to sarcopenia or obesity independently (100).

Ward-Ritacco et al. (14) examined the contribution of body composition, physical activity, muscle capacity and muscle quality to physical function performance in sixty-four post-menopausal women. Body composition was measured with dual-energy X-ray absorptiometry (DXA) and physical function was assessed with the Timed Up and Go test, 30 second chair stand and 6-minute-walk-test (6MWT). Percent fat was found to be an independent predictor of performance in the 6MWT and when muscle quality and total number of health conditions were controlled, adiposity was still significantly associated with 6MWT performance ($p=0.003$). This indicates the important role that adiposity plays in determining functional performance.

Bea et al. (101) also examined the association between body composition (total lean mass and body fat) and physical function in postmenopausal women. Physical function, which was measured subjectively using the SF-36 Questionnaire, declined from baseline to three years of follow-up. An increase of more than 5% in total body fat mass was associated with a greater decline in physical function ($p<0.05$), compared to those with no change in percent body fat. Women with the poorest body composition profiles at baseline (lowest lean mass and highest fat mass), demonstrated

a greater decline in physical function over the course of the study. Interestingly, an increase in lean mass of more than 5%, from baseline to three years of follow-up, was not protective against worsened physical function ($p<0.05$), when compared to those with no change in lean mass. These findings emphasize the importance of assessing body fatness and lean mass, when examining the association between body composition and physical function. Relevant literature on age-related changes in body composition and physical function support the concept that with age, losses in lean mass and increases in fat mass independently play a role in worsened physical function performance.

Body Composition and Muscle Fatigue

The association between body composition and muscular fatigue is not well elucidated. Goncalves et al. (102) investigated the relationship between body composition, muscle fatigue and physical function in a sample of 29 older women (68.2 +/- 7.3 years). Body composition was measured using bioelectrical impedance analysis, muscle fatigue was measured with electromyography during a 60-second sustained isometric knee extension contraction, and physical function was measured using a 10-meter walk test (10MWT), rising from a sitting position (RSP), rising from a ventral decubitus position (RVDP) and rising from a chair and walking about the house (RCWH). There was no significant association between lean mass and muscle fatigue. The small sample size of twenty-nine limits the generalizability of these findings and more research needs to be done to fully understand the relationship between body composition and muscle fatigue. There were similar findings in the

Health ABC study, in which there was no significant correlation found between body composition and fatigue index (64).

The current literature examining the association between muscle fatigue and body composition suggests that there is no significant relationship between body composition and muscle fatigue. More research needs to be done to understand whether age-related changes in body composition may contribute to increased fatigability with age. While changes in body composition with age contribute to a decline in muscle strength (103), this same relationship has not been observed with muscle fatigue. It is unexpected to find a lack of an association between muscle fatigue and body composition, which further emphasizes the independent nature of muscle fatigue and the need to better understand how it contributes to functional decline with age.

Physical Function and Physical Activity

Physical activity refers to any bodily movement that elicits energy expenditure above resting levels. The American College of Sports Medicine (ACSM) recommends that healthy adults between ages 18 and 65 participate in a minimum of 150 minutes of moderate-intensity aerobic physical activity or 75 minutes of vigorous-intensity aerobic physical activity a week, or an equivalent combination, in addition to muscle strengthening exercise for all major muscle groups at a moderate intensity or higher on two or more days of the week (104)(105). Measuring physical activity on the population-level presents with challenges, as more cost-effective measures, such as self-report, can be subject to bias. Objective measures, such as accelerometer use, are more accurate, but are more costly (106). The majority of Americans are not meeting

physical activity recommendations for both aerobic and resistance training and there is a wide range of percentages on how many are achieving the recommended amount of aerobic physical activity ranging from 3.4% to 95.6% (107), due to measurement approach and cut-point criterion. However, it is known that there is a marked decrease in physical activity and an increase in sedentary behavior with age (108)(109) that can have severe implications such as lowered quality of life (110) and an increased risk of disease (111) and mortality (112). Age-related declines in physical activity are impacted by education level, socioeconomic status and psychosocial influences in which those with lower education levels and socioeconomic statuses are more susceptible to greater physical activity depreciation with age (113)(114). This age-related decrease in physical activity is greater in women, and can have implications for physical function (115)(116)(117). Higher levels of vigorous-intensity aerobic physical activity in middle-aged women has been shown to improve body composition (less fat mass, more lean mass) and decrease weight gain associated with menopause (118), in addition to improving psychological well-being and lowering the severity of both vaso-somatic and general somatic menopausal symptoms (119). The improved body composition with increased physical activity levels indicates the mediating role that physical activity also plays in physical function of this population.

In 2016, Middlekauff et al. (120) examined physical activity patterns in healthy middle-aged women around the menopausal transition to assess whether the 2008 Physical Activity Guidelines for Americans were met through leisure, household and outdoor activities. This study measured self-reported physical activity in 440 healthy women ages 51 to 64 years old, with the majority (77.6%) being post-menopausal.

Only 25.91% of this cohort met the recommendation for meeting ACSM guidelines. However, when moderate, vigorous and muscle-strengthening activity was assessed across all domains of physical activity, including household and outdoor activities, 73.41% of this population met the recommendations, which is markedly higher than the observed prevalence of U.S adults. This indicates that PA research on women of middle-age may be under-reporting physical activity, due to the assessment of only leisure-time PA without the assessment of household and outdoor activities. However, this study may be limited by its use of self-report measures of physical activity, which have a high risk of over-reporting and can be subject to bias. Also, the middle-aged women of this cohort were of a relatively high education level, which has limited generalizability to the general population, as education level and socioeconomic status are predictive of physical activity levels (114).

Age-related changes in physical activity contribute to reductions in lean mass and muscle strength of the lower body (121), in addition to deterioration of muscle quality (122). All of these factors increase the risk of developing physical function limitations with age and worsening quality of life in older age.

Physical Function, Muscle Strength and Muscle Quality

Muscle strength has been found to be independently associated with physical function and research demonstrates that there is a significant decline in muscle strength with age (115) and that decreases in physical activity with age and decreased lean mass are contributing factors to the muscle strength declines observed with age (123). Murray et al. (124) examined this muscular strength in healthy women ages 20 to 35 years old, 42 to 61 years old and 70 to 86 years old, who were assessed for knee

extensor and flexor torque using maximum isometric contractions, at 30 degrees, 45 degrees and 60 degrees of flexion, and an isokinetic dynamic task at 36 degrees per second. Across all tasks and knee joint angles, there was a decrease in strength from the youngest group to the oldest group, in which the middle-aged group had 77 to 95% of the strength of the youngest group and the oldest group had 56 to 78% of the strength of the youngest group. This loss of strength with age has implications for physical function performance and may contribute to the increased risk of disability with age (125).

Brill et al. (126) investigated the relationship between muscular strength and the presence of functional limitations at an average follow-up of five years with 3,069 men and 589 women aged 30 to 82 years. At baseline, participants were sorted into high and low strength groups based on a calculated strength and endurance index composite score from their performance on a 1 repetition maximum (1RM) bench press, 1RM leg press and a 60-second sit-up test. This index was calculated with the use of age and gender tertiles to group the participant accordingly based on their strength index. Participants also completed a maximal graded exercise test and were included in analysis if they achieved 85% of their maximum heart rate. Treadmill time on the maximal graded test, which is correlated to maximum oxygen uptake, a measurement of cardiorespiratory fitness, was controlled for in the analysis. When adjusted for age, BMI, treadmill time, number of new health problems since baseline and follow-up year, men that were in the high strength group were about half as likely (OR= .56; CI: .34-.93) to develop a functional limitation as men in the low strength

group. However, while this same trend was identified in women, the odds ratio was not statistically significant, potentially because of the smaller sample size.

Visser et al. (127) examined the association between muscular strength and physical function, as well as the influences of muscle mass on the mobility decline of older adults prospectively over the span of 2.5 years. The incidence of mobility limitations over the course of the 2.5-year follow-up was evaluated through annual clinic evaluations and telephone contacts at 6, 18 and 30 months. With adjustment for age, race, study site, body height, and body fat mass, women in the lowest quartile of muscle strength were 2.15 (95% CI: 1.61-2.87) times more likely to experience mobility limitations, when compared to women of the highest quartile of muscle strength at baseline. Muscle strength was found to be an independent predictor of mobility limitations with age. Interestingly, mid-thigh muscle area was also determined to be associated with incident mobility limitations throughout the 2.5-year follow-up, however, this relationship was not independent of knee extensor muscle strength, indicating the importance of muscle strength in influencing mobility decline with age.

Landers et al. (128) also investigated the interrelationship of muscle strength and muscle mass in the performance of ADLs in 21 older (ages 60-75) and 20 younger (ages 23-34) women with similar BMI. Maximum isometric strength of the knee extensors and elbow flexors was measured by an immediate force measurement feedback of a digital transducer, and integrated electromyography (IEMG) of the rectus femoris and biceps brachii was evaluated. IEMG was also used to assess physical performance of ADLS, in a standing task and a four-minute weight-loaded

walking task. After adjusting for upper leg lean tissue mass, there was a significant inverse correlation between age and maximum knee extension ($R = -.338, p < 0.05$), indicating younger women had higher maximum knee extension strength than the older women in this study cohort. Older women also had more difficulty in their performance of ADLs, seen in their increased highly normalized IEMG (nIEMG) during the standing task, however when adjusted for covariates, there was no significant difference in nIEMG between the older and younger women. This study demonstrated the strength differences between older and younger women and indicated that lower body strength plays an integral role in physical function and activities of daily living.

Barbat-Artigas (129) attempted to identify a muscle index that would be clinically relevant in the identification of older women at risk for functional impairments. Body composition, hand grip and knee extension strength were measured in a cohort of 1,462 women over the age of 75. Physical function was assessed with the repeated chair stands test and gait speed tests at usual and fast pace. Lower body relative muscle strength (LB-RMS), an index of body weight and quadriceps muscle strength, was most highly associated with measures of subjective and objective physical function. It has been well-established across literature that declines in muscle mass and muscle strength with age contribute to the functional decline associated with advanced aging.

Relatedly, muscle quality, defined as muscle strength normalized for lean mass, has become a unique characteristic to examine in association with physical function in middle-aged and older adults (129)(130). Muscle strength and muscle

mass both generally decline with age and contribute to the functional decline associated with advancing age (85)(94). Measures of muscle quality combine both muscle capacity and muscle mass, and as such, this variable may be more highly related to physical function and may be more clinically significant when trying to identify those at risk for functional impairments (129)(131). Research on muscle quality is limited by the lack of a standardized definition for muscle quality, which has led to inconsistent findings (130). While research has identified the independent contribution of muscle quality to physical function decline in older adults (132)(133), there is less understood about this parameter in middle-aged women.

The limited research on muscle quality in middle-aged women preliminarily suggests that muscle quality declines in middle-age (134), and that this can lead to declines in physical function (14). Francis et al. found that women ages 60 to 70 years old had a 8% lower muscle quality than women ages 50 to 59 years old (134). This significant decline in the midlife period could increase the risk of disability and worsened quality of life with advanced age. Ward-Ritacco et al. (14) examined body composition, physical activity, isokinetic muscle strength at 60 degrees per second and muscle quality in sixty-four post-menopausal women. Muscle quality, when calculated with leg strength, steps per day and adiposity, was independently associated with objective physical function performance on the 6MWT. The limited research on women in middle-age suggests that muscle quality declines in midlife and that this is independently associated with worsened physical function performance (14). More research on muscle quality in middle-aged women is needed to further investigate this association.

Conclusion

Research on muscle fatigue, physical activity, physical function and body composition is primarily focused on the older adult population. There is currently very limited research on the interaction of these variables in the middle-age period for women. With rising disability rates in middle-aged women, to the extent that 19% of 56-66-year-old women in one cohort identified as having an extreme mobility disability (2), there is a critical need to fully understand the pathway to physical function limitations and disability specific to this population.

The current, limited, research on women of middle-age indicates that with age, declines in physical activity contribute to an unfavorable shift in body composition (less lean mass, more fat mass), which then plays a role in reducing muscle mass, strength and muscle quality (14). Reductions in muscle mass and strength leads to worsened physical function and increased risk of disability and mortality (85). It is unknown whether muscle fatigue, a unique parameter of muscle function, is a contributing factor to physical function depreciation in middle age. Older populations are seen to develop fatigue resistance in isometric and low-velocity tasks, when compared to younger populations (63)(22), however, this fatigue resistance is reversed in high-velocity dynamic contractions, indicating that contraction speed and type are both critical when investigating muscular fatigue (80). Notably, increased fatigability during high-velocity dynamic contractions is independently associated with the exacerbation of functional declines (19)(28) in very old adults (16). Current research has also shown the concept that muscle fatigue is independent of other measures of muscle function, including strength and quality, which indicates the relevance of

studying muscle fatigue in its independent association to physical function.

Understanding whether muscle fatigue is directly related to functional decline in women of midlife would help in targeted approaches to improve physical function of this under-researched population.

CHAPTER 3

METHODOLOGY

Study Design

The Women's Health Improvement Initiative (WHII), a cross-sectional observational study, began in 2016 under the direction of Principle Investigators, Christie Ward-Ritacco, PhD and Natalie Sabik, PhD. Data were collected on two visits seven to 10 days apart. During the first visit, participants provided informed consent and underwent several objectively measured physical function assessments. Between the first and second visit, participants wore an Actigraph accelerometer (Actigraph GT9XLink, Pensacola, FL) on their hip for all waking hours, except when bathing or swimming, and kept a physical activity log. During the second visit, body composition was measured. Isometric knee strength for isometric knee extension/flexion at 60 degrees, isokinetic knee extension/flexion at 60 degrees per second and 180 degrees per second was assessed, and a dynamic fatiguing task for knee extension/flexion was completed.

Participants

A sample size of 109 participants was determined to appropriately assess the study aim of examining the association between muscle fatigue index and physical function and achieve significance with a *p*-value of less than 0.05, a medium effect size of 0.3, and a power of 0.9 with a 2-tailed correlation (G Power). To account for potential participant dropout, 120 participants were recruited. This sample size is

similar to those used in other research studies examining the association between muscular fatigue and physical function (62). The study recruited a convenience sample of middle-aged women between the ages of 40 and 64 years old and participants were recruited by word-of-mouth, social media postings, and flyers posted at the University of Rhode Island and in the surrounding area. Interested participants were assessed for inclusion and exclusion criteria via an eligibility survey and eligible women completed two experimental visits. Inclusion criteria included being female, being 40-64 years, having the ability to speak and read English, and having a BMI between 18.5 and 45.0 kg/m². Participants also had to be willing to undergo a dual energy X-ray absorptiometry (DXA) scan and be living independently. Exclusion criteria included affirmatively answering any of the questions on the Physical Activity Readiness Questionnaire (PAR-Q), a Mini Mental State Examination (MMSE) score below 25, being a smoker, being pregnant, having weight instability (>5-pound changes in body weight over the past 3 months) and/or any pre-existing conditions that would impact their safe completion of any of the study procedures. Pre-existing conditions that may impact safe completion included uncontrolled cardiovascular disease or chronic obstructive pulmonary disease, recently experienced cardiovascular event, uncontrolled diabetes mellitus type I or type II, and/or severe musculoskeletal disorders.

Physical Function Assessments

Several objective assessments were used to measure physical function. Prior to data collection, the research team met regularly to ensure that all members were thoroughly trained on how to properly administer all objective physical function

assessments and a set script was utilized by all test administrators when conducting assessments to ensure consistency and improve inter-rater reliability. Physical function measures included the transfer task, 30 second chair stand, 6-minute walk test (6MWT), 8 foot up and go, and lift and carry. Standardized equipment used included cones, an armless chair, tape, a surveyor's wheel, a stopwatch, a mat, a crate with a 10-pound weight, and a 3.5-foot shelf. Each task was separated by two minutes of rest or longer to ensure fatigue from one assessment did not interfere with the following activity. Rating of perceived exertion (Borg Scale 6-20) and pain and fatigue scales (0-10) were used to assess participant exertion on each task. The Borg Scale has been validated as a measure of relative aerobic exercise intensity (135). Participants were instructed to work to the best of their ability, and they had the option to complete a second trial of an activity if they felt they could improve upon their initial performance.

- Transfer task: The transfer task is a reliable and valid measure for assessing dynamic physical function, as determined by floor-transfer ability (136). Participants began in a standing position and were instructed to transfer to a sitting position on a floor mat (ensuring full contact of their buttocks with the floor) and then return to a standing position as quickly and safely as possible. The time to complete the task was recorded. Participants completed this task twice and the best time was used for analysis.
- 30 second chair stand: An armless chair was set up against the wall. With their hands on the opposite shoulder, participants were instructed to rise from a seated position to a full standing position and return to the seated position

(ensuring full contact of their buttocks with the chair) as many times as possible in 30 seconds. The score was the number of times the participant came to a full standing position. The 30 second chair stand test is a valid measure of lower body strength (137), and physical function. Participants completed this task twice and the highest number of repetitions was used for analysis.

- 6-Minute Walk Test: The 6MWT measured the distance that the participant was able to walk over a total of six minutes using a preset 30-meter course. The participant was instructed to walk as quickly as possible for 6 minutes around the preset course. Members of the research team provided encouragement to the participant at regular intervals using similar phrases. Participants were instructed to pace themselves and reminded that they could take breaks as needed. The total distance covered [(distance of each pass * total number of passes) + partial pass distance] was recorded. The 6MWT has been validated as a measure of physical endurance and physical function in older adults (138).
- 8 Foot Up and Go: The 8 foot up and go is a valid measure for assessing functional performance (139). An armless chair was set against a wall with a cone placed 8 feet in front of the chair. Participants were instructed to stand up from the chair, without using their arms, walk as quickly and as safely around the cone as possible, walk back to the chair and sit down. Total time needed to complete the task was recorded. Participants performed this task twice and the best time was included in the analysis.

- **Lift and Carry:** A 3.5 ft shelf was placed against a wall and the researcher measured ten feet in front of the shelf with a surveyor's wheel and placed a piece of tape to set the course. At the start of the course (where a strip of tape was placed as the starting line), a milk crate with a ten-pound weight inside was placed on the ground. A research team member demonstrated the assessment for participants and asked that participants pick up the weighted crate from the floor using proper form, walk ten feet, place the crate on a 3.5 ft. shelf, remove their hands from the crate, pick the crate back up and return to the start of the course and return the crate to the ground. The time to complete the lift and carry task five times was recorded.
- **Lower extremity physical function composite score (LEPF-CS) (132):** The LEPF-CS was calculated using Z scores from the four lower extremity physical function tasks (transfer task, 8 foot up and go, 30 second chair stand and 6MWT) using SPSS statistical software. In physical function tests like the 8 foot up and go and the transfer task where a lower time is indicative of better physical function, the inverse of the Z score was computed. The LEPF-CS is the total of the four computed Z-scores.

Physical Activity Assessment

Participants wore an Actigraph accelerometer (GT9XLink, ActiGraph, LLC, Pensacola, FL, USA) on their hip for 7-10 days between visit 1 and visit 2.

Participants were instructed to wear the accelerometer for all waking hours, except when bathing or swimming.

Triaxial accelerometers from Actigraph have been validated to measure physical activity when compared to oxygen consumption (140). Physical activity was measured by total steps per day, total minutes of physical activity per day, and total minutes of moderate to vigorous physical activity per day. Valid wear time criteria for inclusion in the final analysis was ten hours per day for a minimum of four days.

In addition to wearing the accelerometer, participants also tracked their physical activity using a physical activity log, which was utilized in assessing resistance training participation. Self-reported resistance training was coded in two ways: 1) meeting resistance training physical activity (PA) guidelines of two or more days of muscle strengthening exercise focused on all major muscle groups (104), and 2) completing any resistance training (one session or more) during the observation period.

Body Composition Assessment

Weight (kg) was measured with a digital scale (Tanita WB-100, Arlington Heights, IL) and height (cm) was measured with a stadiometer (Seca 213, Chino, CA). Body mass index (BMI) was calculated as weight (kg) divided by height (m^2). Body composition was assessed using DXA (GE Lunar iDXA, Waukesha, WI, USA). DXA is a validated method for assessing body composition (141). Participants wore medical scrubs if their clothing contained reflective material, zippers, and/or buttons, and removed all jewelry prior to the DXA scan. Premenopausal participants took a pregnancy test to ensure that they were not pregnant. A qualified professional performed the DXA scan in compliance with Rhode Island mandated laws.

Muscle Strength and Muscle Quality Assessment

The Biodex Isokinetic System 4 Dynamometer (Shirley, NY, USA) was used to assess muscular strength and fatigue. The Biodex Isokinetic Dynamometer has been validated to assess torque across different velocities (142). Isokinetic dynamometers have high test-retest reliability in assessing isokinetic peak torque and work, specifically in knee extension and flexion (143). Bilateral knee strength was assessed in three ways: 1) 3 sets of isometric knee flexion and extension at 60 degrees (5 second hold) (PT-Isometric-60), 2) 2 sets of 4 repetitions of isokinetic knee flexion and extension at 60 degrees/second (PT-60), and 3) 2 sets of 4 repetitions of isokinetic knee flexion and extension at 180 degrees/second (PT-180). The left and right legs were assessed at both 60 and 180 degrees/sec in a randomized fashion. Peak torque was calculated for PT-Isometric-60, PT-60 and PT-180 by summing the trials that had the greatest torque for the right and left sides. These trials also served as familiarization to using the Biodex before the fatiguing task. Ample rest time of 30 to 90 seconds was given between each set and 3 minutes of rest was provided before the fatiguing task.

Muscle quality was calculated as muscle strength normalized for upper leg lean mass (muscle strength/lean mass). Upper leg lean mass was summed for the right and left legs and muscle quality was assessed in three ways: 1) Isometric-60 normalized for upper leg lean mass (MQ-Isometric-60), 2) Isokinetic-60 normalized for upper leg lean mass (MQ-60) and 3) Isokinetic-180 (MQ-180) normalized for upper leg lean mass.

Muscle Fatigue Assessment

To assess muscular fatigue, participants were asked to perform 25 repetitions of knee flexion/extension at 180 degrees per second. Participants were instructed to exert maximal force from the start and were asked to “kick as hard and as fast as you can throughout the repetitions”. Torque, in Nm, was collected throughout all repetitions. Muscular Fatigue Index was then calculated by calculating the percentage peak torque difference from the first 3 repetitions to the last 3 repetitions. This MFI formula has been used in studies with similar fatiguing protocols (64)(59)(61) and reflects torque decline over the course of the task, indicating fatigue resistance. Participants with an MFI over 100% were considered to have an invalid fatigue task and were not included in the analysis, as an MFI over 100% indicates that the participant may have been pacing, as the force of contraction increased through the task.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 26.0 (IBM Corp, Armonk, NY) and statistical significance was set at $p \leq 0.05$. All data were examined for normality via skewness and kurtosis to ensure normal distribution. Descriptive statistics (mean $\pm$ SD) were calculated. ANOVA was used to determine if there were significant differences in MFI by menopausal group (premenopausal, perimenopausal, postmenopausal). Bivariate correlation analysis was used to determine if there was a significant association between MFI and measures of physical function (transfer task, 30 second chair stand, 6MWT, 8 foot up and go, lift and carry and LEPF-CS). Additionally, bivariate correlation was used to assess the strength of the association

between physical function performance and hypothesized control variables, including age, body fat, physical activity (MVPA per day), isokinetic strength (PT-180) and muscle quality (MQ-180) on measures of physical function. Partial correlation analysis examining MFI and all measures of physical function performance, controlling for age, body fat, MVPA per day and MQ-180, were also completed.

Finally, hierarchical linear regression analysis examined the influence of MFI and control variables, including age, body fat, physical activity, muscle quality, and resistance training, on measures of physical function. Resistance training utilized in this model was classified as one or more training sessions of RT recorded in their PA log. Stepwise regression analyses were performed in the following order: Step 1: age; Step 2: age and %body fat; Step 3: age, %body fat, MVPA per day, Step 4: age, %body fat, MVPA per day, MQ-180, Step 5: age, %body fat, MVPA per day, MQ-180, RT and Step 6: age, %body fat, MVPA per day, MQ-180, RT, MFI. The final step is reported in Table 5.

CHAPTER 4

FINDINGS

There were 180 women screened for eligibility. Eleven were deemed ineligible due to being a smoker (n=2), not living independently (n=1), having a BMI over 40 kg/m² or weight instability (n=7), or severe musculoskeletal disorder (n=1). Thirty-eight women did not respond to follow-up contact, which left 131 eligible participants. Of these eligible participants, four did not attend visit 1 and two did not complete visit 2 due to time availability. Nine were excluded from data analysis due to missing data and 12 were excluded from the analysis due to having an MFI over 100, which indicated pacing throughout the fatiguing task. Therefore, 104 participants were included in the final analysis.

Descriptive characteristics and physical function outcomes are included in Table 1, including characteristics by menopausal status group: premenopausal (n=22), peri-menopausal (n=27), and post-menopausal (n=55). The average age for the sample was 52.9 (± 6.1) years old and average BMI was 26.4 (± 5.1) kg/m². Muscle strength, muscle quality, and MFI values are shown in Table 2. Figure 1 shows MFI by menopausal status group. There were no significant differences between menopausal status groups, however there was a non-significant trend towards increased fatigue resistance with menopausal group, such that post-menopausal women had the highest fatigue resistance.

Bivariate correlation analyses were used to evaluate the strength of the association between measures of physical function and age, percent body fat, MVPA per day, PT-180 and MQ-180, and MFI (Table 3). Transfer task performance was significantly associated with age ($r=.24$), percent body fat ($r=.45$), MVPA ($r=-.25$), PT-180 ($r=-.37$), MQ-180 ($r=-.45$) and MFI ($r=.26$) (all $p \leq 0.05$). Thirty second chair stand task performance was significantly associated with percent body fat ($r=-.31$), MVPA ($r=.29$), PT-180 ($r=.20$), MQ-180 ($r=.34$) (all $p \leq 0.05$). Six-minute walk test performance was associated with percent body fat ($r=-.46$), MVPA ($r=.38$), PT-180 ($r=.27$), MQ-180 ($r=.44$) (all $p \leq 0.001$). Performance on the 8 foot up and go task was significantly associated with percent body fat ($r=-.26$, $p \leq 0.001$) and MVPA ($r=-.207$, $p \leq 0.05$). The lift and carry was significantly correlated with percent body fat ($r=.23$), MVPA ($r=-.26$), PT-180 ($r=-.34$), MQ-180 ($r=-.41$), and MFI ($r=.20$) (all $p \leq 0.05$). Finally, LEPF-CS was significantly associated with percent body fat ($r=-.49$), MVPA ($r=.37$), PT-180 ($r=.35$), MQ-180 ($r=-.48$), and MFI ($r=-.21$) (all $p \leq 0.05$).

To further explore the contribution of MFI to physical function performance, partial correlation analyses controlling for age, percent body fat, MVPA, and MQ-180 were completed (Table 4). When controlling for these variables, MFI was only significantly associated with transfer task performance ($r=.26$, $p \leq 0.05$), and there was no longer a statistically significant association between MFI and performance in the lift and carry task or LEPF-CS.

Table 5 provides the results from the multiple linear regression analyses, examining the independent associations between the physical function tasks and age, percent body fat, MVPA, MQ-180, RT, and MFI. The first regression analysis

demonstrated that faster transfer task performance was associated with younger age ($p=0.008$), lower percent body fat ($p=0.001$), higher levels of MVPA ($p=0.05$) and lower MFI ($p=0.02$). Both MQ-180 ($p=0.08$) and RT ($p=0.79$) were not significantly associated with transfer task performance.

Regression analysis for 30 second chair rise performance indicated that better chair rise performance, or more repetitions during the 30 second task, was significantly associated with higher levels of MVPA ($p=0.03$) and explained 4.6% of the variance in 30 second chair rise performance. Age ($p=0.27$), percent body fat ($p=0.11$), MQ-180 ($p=0.08$), RT ($p=0.67$) and MFI ($p=0.95$) were not associated with 30 second chair rise performance.

Greater distance walked during the 6MWT was significantly associated with lower percent body fat ($p=0.02$), higher levels of MVPA ($p=0.004$), and better MQ-180 ($p=0.03$). Percent body, MVPA and MQ-180 accounted for 20.4% 7.5% and 7.6% of the variance in 6MWT, respectively. Age, RT and MFI were not significantly associated with 6MWT (all $p>0.05$).

The model including age, percent body fat, MVPA, MQ-180, RT and MFI did not significantly explain variance in 8 foot up and go performance ($F_{5,98}=2.706$, $p=0.064$), as there were no significant associations between these variables and 8 foot up and go performance. Better lift and carry task performance was only significantly associated with better MQ-180 ($p=0.015$), with MQ-180 contributing to 13.3% of the variance in task performance.

More optimal LEPF-CS was found to be significantly associated with younger age ($p=0.04$), lower percent body fat ($p=0.001$), higher levels of MVPA ($p=0.002$) and

better MQ-180 ($p=0.040$). Percent body fat was the most significant contributor, as it accounted for 25.1% of the variance in LEPF-CS.

CHAPTER 5

CONCLUSION

There are several well-established contributors to physical performance, including age, percent body fat, physical activity level, muscle strength and muscle quality (15)(14)(101). The present study evaluated the strength of the association between muscle fatigue, using the MFI, and physical function in comparison to these other known contributors. The findings demonstrate that while there is a small, but significant, association between MFI and some objectively measured physical function tasks, the strength of this association decreased when other independent variables, such as percent body fat, muscle quality and physical activity, were included in the analysis. This indicates that the role of muscle fatigue in physical function is modulated by other more strongly related factors such as percent body fat, muscle quality and MVPA.

The results of this study refute the hypothesis that higher MFIs, indicating better fatigue resistance, are associated with better physical function performance. When controlling for age, percent body fat, muscle quality and MVPA per day, MFI was only found to be associated with the transfer task, such that higher MFI, indicating more fatigue resistance, was correlated to slower transfer task performance. While this finding was contrary to our hypothesis, it is possible that this is due to the nature of the transfer task, as an individual's performance on this assessment may be highly dependent on their ability to generate muscle power (144). Fatigue resistance

could be reflective of greater type I muscle fiber activation, which may be related to the reduced ability to generate muscle power. Since the transfer task is reliant on anaerobic metabolism and the ability to generate power rapidly, it is possible that those who have better anaerobic power would have more optimal transfer task performance but also be more prone to fatigue. While this may be biologically plausible, muscle power was not directly measured in the current study. Therefore, we can only hypothesize that muscle power is related to transfer task performance in our sample, and therefore fatigue would be inversely related to performance on the transfer task, a task requiring power-based muscular contractions.

There is limited literature available examining the association between muscle fatigue and physical function in adults (62)(19). Silva et al. (62) examined the association between physical function and muscle fatigue in 135 older women (>65 years old) and found a significant negative correlation between MFI, measured with 21 maximal knee extension repetitions at 180 degrees/second, and sit-to-stand score. The finding that poorer physical function is associated with increased fatigue resistance is similar to the outcome of the current study, though Silva et al. (62) did not control for body fat, physical activity level, and muscle quality. The sit-to-stand task may rely similarly on quick high-intensity power-based movement, similar to the transfer task used in the current study, thus explaining the similarity in the results.

In contrast, Senefeld et al. (19) found that increased muscle fatigue, as measured by a muscle fatiguing task of 90 maximal effort knee flexion and extension contractions at 20% of maximum voluntary isometric contraction, was associated with poorer physical function, as measured by 6MWT and a balance score. Senefeld et al.

(19) did not measure or control for other potential confounding variables, such as percent body fat and muscle quality, which were more highly associated with PF compared to muscle fatigue in the present study. Secondly, the fatigue inducing protocol utilized by Silva et al. (62) was significantly more demanding than the protocol utilized in the current study, which contribute to the differences in our findings. Finally, the sit-to-stand task used by Silva et al. (62) and the transfer task in the present study are physical function tasks that rely primarily on muscular power, while the physical function assessments utilized by Senefeld et al. (19) study require greater muscular endurance. The different components of physical fitness needed for successful completion of these types of function tasks may explain why Senefeld et al. (19) found a significant association between muscle fatigue and physical function and the present study did not.

To our knowledge there are no available studies examining the association between muscle fatigue and physical function in middle-aged women. There are a small number of studies available using older adults that have found that greater fatigability during high-velocity knee flexion and extension is associated with poorer physical function performance (19)(28). Therefore, it would be plausible to expect that greater fatigability would be associated with poorer physical function performance in middle-aged women. The contraction speed chosen for the muscular fatiguing task in this present study, 180 degrees per second, may have been too slow to elicit fatigue similar to that experienced by older adults in studies utilizing fatiguing tasks with faster contractions speeds (19)(28). Selecting a fatiguing task with a higher velocity may more closely simulate the speed associated with the completion of

related ADLs (84) and selected measures of physical function. The lack of a clear association between MFI and most of the physical function assessments utilized in this study may also be due to physical function test selection. While the objective measures used to assess physical function have been validated for use in older populations, it is possible that these measures aren't sensitive to the smaller differences in physical function that may appear in middle-aged persons. There is a need for more clinically sensitive measures of physical function assessment for middle-age populations. As discussed earlier, physical function decline in middle-age may be more subtle and before experiencing self-reported difficulty with a function task, middle-aged populations may modify the task by using compensatory strategies and using a slower walking pace (13).

The present study supports results from previous work on middle-aged women that identified the independent contributions of physical activity level, percent body fat (15) and muscle quality (14) to physical function, however, those studies did not evaluate the role of muscle fatigue. Evidence from the present study found that muscle quality, body fat and physical activity were more highly associated with physical function compared to muscle fatigue, similar to the findings of Ward-Ritacco et al. (14) in which muscle quality, adiposity, and physical activity were all significant contributors to physical function performance. The 6MWT in the present study was most sensitive to differences in percent body fat, MVPA and MQ, which also supports findings from Ward-Ritacco et al. (14), in which number of medical conditions, muscle quality, steps per day and adiposity were significant predictors of performance in the 6MWT. The present findings also align with longitudinal findings from Bea et

al. (101) which found that women with lower percentages of lean mass and higher percentages of fat mass experienced the most functional decline over three years. Increased fat mass, which is metabolically active and is associated with inflammatory factors (145), could potentially play a role in poorer muscle quality in middle-aged women, as this mechanism has been identified in older adult populations (146). Additionally, women who are physically active are less susceptible to age-related changes in body composition (147)(148) and are better able to maintain muscle quality with advancing age (149). There is an interaction of increased body fat, worsened muscle quality and lowered physical activity levels which can lead to physical function decline, however more research is necessary to fully elucidate this mechanism.

When evaluating the current findings, it is important to examine the generalizability of this sample to the population of middle-aged women, as the health status of the participants may play a significant role in our findings. Women in the present study achieved 31.05 minutes per day activity (± 23.52 minutes) of MVPA moderate to vigorous physical, which is a similar amount to that achieved by other samples of middle-aged adults (27.7 ± 20.9 minutes(150) 29.2 ± 0.8 minutes (151)). When examining percent body fat and BMI, the women in the present study had an average percent body fat of 38.25% (± 7.91) and BMI of 26.38 (± 5.10) kg/m², which are both lower than the reference standards for women aged 40-69 (152)(153). These results suggest that the present sample of women has a healthier body composition than other, larger samples of middle-aged women. This warrants further research to examine physical function performance in a more generalizable sample.

While muscle fatigue was not found to be significantly associated with the objectively measured physical function tasks utilized in the current study, it was confirmed that percent body fat, physical activity level, and muscle quality are independently associated with physical functional performance. Specifically, percent body fat was highly associated with all of the function tasks, underlying the importance of measuring this variable in middle-aged women and identifying it as the potential factor for intervention when planning future research in this area. Therefore, the findings of this study support the use of interventions aimed to lower fat mass and increase lean mass for middle-aged women. These findings also provide evidence highlighting the importance of moderate to vigorous physical activity in reducing the risk of physical function limitations, indicating the importance of physical activity in midlife particularly in improving functional status outcomes.

Additionally, each physical function task had a different independent variable most highly associated with it; the 30 second chair rise performance was most highly associated with MVPA, the 6MWT was most highly associated with percent body fat, and the lift and carry was most highly associated with MQ-180. These findings substantiate the importance of the principle of specificity and emphasizes that the most highly associated independent variable reflects the aspect of physical fitness reflected in the nature of the physical function task. This continues to highlight that physical function is multi-faceted and optimal performance will be dependent on multiple factors.

The present study has several strengths, including the objective measurement of physical activity and an objective battery of validated physical function

measurements. Objectively measuring both of these variables limits self-report bias and decreases the risk to validity associated with subjective measures of physical activity (154) and physical function (155). The use of DXA to examine body composition (141) is another strength of this study. Furthermore, while the primary outcome measures were MFI and physical function, this study was comprehensive in controlling for other variables previously identified as contributors to physical function in this population.

There are also limitations of the present study. First, the cross-sectional nature of the study does not lend itself to examining the directionality of any of the associations discovered. Additionally, the sample was recruited through a convenience sampling technique, and the participants were predominantly Caucasian, educated, and able-bodied women with no orthopedic limitations. These women sampled were also leaner than the general population of middle-aged based on percent body fat measurements, which may limit the generalizability to the larger context of middle-aged women.

As stated earlier, the contraction speed of 180 degrees per second for the fatiguing task may have been too low to elicit the fatigue response necessary to assess in its association to physical function in this population. Utilizing a higher-velocity contraction speed may be more representative of the velocity necessary for completion of physical performance tasks throughout the day. This also highlights the need for more standardized methods of fatigue assessment in the laboratory setting and for those methods to be more applicable and generalizable to the fatigue experienced over

the course of the day (84). The variability in muscle fatigue measures may be partially responsible for the discrepancies seen in the literature.

Muscle power was not evaluated in this study. Our findings suggest that transfer task performance may be associated with anaerobic power and therefore may be inversely related to muscle fatigue. However, since muscle power was not directly measured in this study, we cannot definitively identify muscle power as the mechanism for this finding.

Additionally, while aerobic PA (MVPA, steps per day) was assessed objectively using accelerometry, we were unable to calculate the volume of daily and weekly resistance training, limiting our ability to assess the contribution that regular resistance training can make to the examined variables of interest. Finally, in future research, it may be advisable to utilize structural equation modeling (SEM) to analyze the interaction of percent body fat, physical activity and muscle quality, to better understand physical function in this population.

In conclusion, additional research is needed to fully understand the interactive and independent contribution of muscle fatigue to physical function performance in middle-aged women. Further understanding the independent contributions of body composition, physical activity, muscle quality, and muscle fatigue, with physical function in middle age could lead to more optimal targeted interventions delivered in middle-age with the intention of improving health-related outcomes as women transition to older adulthood.

TABLES

Table 1. Participant characteristics

Demographics	Sample Mean $\pm$ SD (n = 104)	Range	Pre- Menopausal (n = 22)	Peri- Menopausal (n = 27)	Post- Menopausal (n = 55)	P
Age (years)	52.93 $\pm$ 6.10	40.00 – 64.00	46.05 $\pm$ 3.39	49.74 $\pm$ 3.79	57.25 $\pm$ 4.02	<0.001
Height (m)	1.63 $\pm$ 0.06	1.51 – 1.78	1.65 $\pm$ 0.06	1.65 $\pm$ 0.05	1.62 $\pm$ 0.05	.095
Weight (kg)	70.55 $\pm$ 14.75	44.30 – 118.30	72.54 $\pm$ 14.77	74.98 $\pm$ 17.64	67.59 $\pm$ 12.64	.079
Natural Waist Circumference (cm)	83.05 $\pm$ 11.24	64.50 – 117.70	82.08 $\pm$ 9.89	85.96 $\pm$ 12.82	82.01 $\pm$ 10.86	.297
Umbilicus Waist Circumference (cm)	91.98 $\pm$ 12.45	67.20 – 130.20	91.91 $\pm$ 10.76	94.29 $\pm$ 13.79	90.87 $\pm$ 12.46	.510
Body mass index (kg/m ²)	26.38 $\pm$ 5.10	17.63 – 42.93	26.66 $\pm$ 5.05	27.62 $\pm$ 5.90	25.67 $\pm$ 4.65	.259
Body fat (%)	38.25 $\pm$ 7.91	18.99 – 53.00	37.06 $\pm$ 7.98	38.52 $\pm$ 7.65	38.56 $\pm$ 8.12	.747
Lean mass (%)	61.75 $\pm$ 7.91	47.01 – 81.01	62.94 $\pm$ 7.98	61.48 $\pm$ 7.65	61.44 $\pm$ 8.12	.747
Physical Activity: Steps/day	8064 $\pm$ 3324	2183 – 20302	7924 $\pm$ 2851	7117 $\pm$ 2713	8551 $\pm$ 3691	.211
Physical activity: MVPA per day (min)	31.05 $\pm$ 23.52	1.00 – 106.67	31.79 $\pm$ 21.29	22.52 $\pm$ 20.49	34.61 $\pm$ 25.05	.069
Physical Function	Mean $\pm$ SD	Range				
Transfer Task (sec)	3.92 $\pm$ 1.19	1.53 – 8.19	3.62 $\pm$ 1.27	3.85 $\pm$ 1.19	4.08 $\pm$ 1.15	.283
30 Second Chair Stand (repetitions)	20.47 $\pm$ 5.41	10.00 – 38.00	21.09 $\pm$ 5.86	20.89 $\pm$ 5.90	20.02 $\pm$ 5.02	.663
6 Minute Walk (m)	576.59 $\pm$ 68.99	429.30 – 734.31	573.40 $\pm$ 75.72	583.07 $\pm$ 58.56	574.64 $\pm$ 72.06	.851
8 foot Up and Go (sec)	5.18 $\pm$.93	2.22 – 7.37	5.03 $\pm$ 1.13	5.10 $\pm$ 0.80	5.28 $\pm$ 0.90	.519
Lift and Carry (sec)	58.43 $\pm$ 11.13	38.84 – 104.96	57.14 $\pm$ 11.66	58.12 $\pm$ 13.51	59.09 $\pm$ 9.73	.778
LEPF-CS	-0.005 $\pm$ 3.05	-9.06 – 8.34	0.46 $\pm$ 3.19	0.37 $\pm$ 2.95	-0.36 $\pm$ 3.05	.464

Data is presented as mean $\pm$ SD unless stated otherwise.

MVPA = moderate to vigorous physical activity.

p-value for menopausal status group differences, determined by ANOVA

Table 2. Muscle Characteristics

Muscle Characteristics	Sample Mean $\pm$ SD (n = 104)	Range	Pre-Menopausal (n = 22)	Peri-Menopausal (n = 27)	Post-Menopausal (n = 55)	P
PT-Isometric-60 (NM)	344.55 $\pm$ 78.41	175.60 – 632.70	382.73 $\pm$ 108.67	355.65 $\pm$ 58.88	323.83 $\pm$ 66.13	.007
PT-60 (NM)	319.80 $\pm$ 68.64	167.30 – 518.50	360.25 $\pm$ 83.74	333.46 $\pm$ 49.33	296.92 $\pm$ 61.61	<0.001
PT-180 (NM)	228.53 $\pm$ 46.92	131.20 – 341.20	257.08 $\pm$ 50.78	243.57 $\pm$ 38.36	209.72 $\pm$ 41.01	<0.001
MQ-Isometric-60	34.80 $\pm$ 6.78	19.41 – 53.64	36.13 $\pm$ 8.37	34.13 $\pm$ 5.30	34.62 $\pm$ 6.82	.577
MQ-60	32.25 $\pm$ 5.57	18.71 – 51.30	34.28 $\pm$ 6.73	32.09 $\pm$ 4.93	31.55 $\pm$ 5.29	.158
MQ-180	23.09 $\pm$ 4.01	12.76 – 34.13	24.56 $\pm$ 4.29	23.48 $\pm$ 4.07	22.34 $\pm$ 3.75	.080
MFI (%)	68.98 $\pm$ 9.76	47.42 – 95.57	66.29 $\pm$ 10.93	68.98 $\pm$ 8.69	70.06 $\pm$ 9.74	.313

PT-Isometric-60 (Peak Torque isometric knee flexion and extension at 60 degrees); PT-60 (Peak Torque isokinetic knee flexion and extension at 60 degrees per second); PT-180 (Peak Torque isokinetic knee flexion and extension at 180 degrees per second); MQ-Isometric-60 (Muscle Quality calculated using peak torque for isometric knee flexion and extension at 60 degrees); MQ-60 (Muscle Quality calculated using peak torque for isokinetic knee flexion and extension at 60 degrees per second); MQ-180 (Muscle Quality calculated using peak torque for isokinetic knee flexion and extension at 180 degrees per second); MFI (Muscle Fatigue Index) *p*-value for menopausal status group differences, determined by ANOVA

Table 3. Pearson correlations between MFI, Age, %Fat, MVPA, PT-180, MQ-180 and objectively measured physical function performance.

	AGE	%FAT	MVPA	PT-180	MQ-180	MFI	SIT	CHR	6MWT	TUG	LIFT	LEPF-CS
AGE	1.0	-.013	.097	-.487**	-.161	.120	.244*	-.140	-.034	.136	.090	-.174
%FAT		1.0	-.271**	-.082	-.416**	-.013	.449**	-.313**	-.457**	.259**	.229*	-.494**
MVPA			1.0	.129	.144	.081	-.251*	.287**	.381**	-.207*	-.257*	.366**
PT-180				1.0	.679**	-.320**	-.367**	.196*	.274**	-.134	-.335**	.345**
MQ-180					1.0	-.473**	-.454**	.341**	.435**	-.118	-.414**	.483**
MFI						1.0	.263**	-.088	-.123	-.084	.200*	-.213*
SIT							1.0	-.545**	-.515**	.268**	.540**	-.764**
CHR								1.0	.447**	-.376**	-.541**	.804**
6MWT									1.0	-.400**	-.596**	.773**
TUG										1.0	.405**	-.657**
LIFT											1.0	-.668**
LEPF-CS												1.0

Age (years of age); %Fat (whole body adiposity); MVPA (moderate to vigorous physical activity per day); PT-180 (peak torque for isokinetic knee flexion and extension at 180 degrees/second); MQ-180 (Muscle Quality calculated using peak torque for isokinetic knee flexion and extension at 180 degrees/second); MFI (muscle fatigue index); SIT (transfer task); CHR (30 second chair stand); 6MWT (6-minute walk test); TUG (8 foot up and go); LIFT (lift and carry); LEPF-CS (lower-extremity physical function composite score)

* $p \leq 0.05$; ** $p \leq 0.001$

Table 4. Partial correlations between muscle fatigue index (MFI) and physical function assessments, when controlling for age, percent body fat, MVPA and MQ-180.

	MFI	SIT	CHR	6MWT	TUG	LIFT	LEPF-CS
MFI	1.0	.260*	-.080	-.048	-.059	.161	-.116
SIT		1.0	-.428**	-.262*	.046	.384**	-.631**
CHR			1.0	.251*	-.309*	-.422**	.752**
6MWT				1.0	-.269*	-.453**	.652**
TUG					1.0	.331**	-.633**
LIFT						1.0	-.593**
LEPF-CS							1.0

MFI (muscle fatigue index); Age (years of age); Percent Body Fat (whole body adiposity); MVPA (moderate to vigorous physical activity per day); MQ-180 (Muscle Quality calculated using peak torque for isokinetic knee flexion and extension at 180 degrees/second); SIT (transfer task); CHR (30 second chair stand); 6MWT (6-minute walk test); TUG (8 foot up and go); LIFT (lift and carry); LEPF-CS (lower-extremity physical function composite score) * $p \leq 0.05$; ** $p \leq 0.001$

Table 5. Regression Analysis Summary for Variables Associated with Physical Function Performance

Variables	B	SEB	<i>p</i>	β	95% CI
(a) Transfer Task ($R^2 = .395, p < .001$)					
Age	.04	.02	.008	.210	[-.01, .07]
% Fat	.05	.01	.001	.319	[-.02, .07]
MVPA	-.01	.004	.050	-.17	[-.02, .00]
MQ-180	-.06	.03	.083	-.197	[-.12, .01]
RT	-.07	.25	.793	-.024	[-.55, .43]
MFI	.03	.01	.024	.225	[-.004, .05]
(b) 30 Second Chair Stand ($R^2 = .203, p = .002$)					
Age	-.09	.09	.271	-.106	[-.26, .08]
% Fat	-.12	.08	.109	-.178	[-.27, .03]
MVPA	.05	.02	.029	.220	[-.01, .10]
MQ-180	.30	.17	.079	.229	[-.04, .64]
RT	.56	1.32	.671	.044	[-2.06, 3.18]
MFI	-.004	.06	.953	-.007	[-.127, .120]
(c) 6-minute Walk Test ($R^2 = .360, p < .001$)					
Age	-.17	.98	.864	-.015	[-2.12, 1.78]
% Fat	-2.18	.88	.015	-.251	[-3.92, -.44]
MVPA	.78	.26	.004	.265	[-.26, 1.31]
MQ-180	4.40	1.99	.030	.261	[-.45, 8.36]
RT	-10.20	15.30	.507	-.062	[-40.59, 20.20]
MFI	-.41	.75	.586	-.056	[-1.91, 1.09]
(d) 8 Foot Up and Go ($R^2 = .120, p = .064$)					
Age	.03	.02	.081	.178	[-.003, .06]
% Fat	.02	.01	.065	.216	[-.002, .05]
MVPA	-.01	.004	.141	-.155	[-.01, .002]
MQ-180	-.01	.03	.665	-.059	[-.07, .05]
RT	-.10	.23	.663	-.048	[-.55, .35]
MFI	-.01	.01	.603	-.062	[-.03, .02]
(e) Lift and Carry ($R^2 = .239, p < .001$)					
Age	.03	.17	.857	.017	[-.31, .37]
% Fat	.01	.15	.951	.007	[-.29, .31]
MVPA	-.09	.05	.055	-.189	[-.18, .002]
MQ-180	-.85	.34	.015	-.313	[-1.52, -.17]
RT	2.25	2.63	.395	.087	[-2.98, 7.47]
MFI	.15	.12	.239	.131	[-.10, .39]
(f) LEPF-CS ($R^2 = .425, p < .001$)					
Age	-.09	.04	.037	-.174	[-.17, -.01]
%Fat	-.13	.04	.001	-.339	[-.20, -.06]
MVPA	.04	.01	.002	.271	[-.01, .06]
MQ-180	.18	.08	.040	.233	[-.01, .34]
RT	.20	.64	.748	.028	[-1.06, 1.47]
MFI	-.01	.03	.296	-.103	[-.10, .03]

Note. Age (years of age); % Fat (whole body adiposity); MVPA (moderate to vigorous physical activity per day); MQ-180 (Muscle Quality calculated using peak torque for isokinetic knee flexion and extension at 180 degrees/second), RT (participants self-reporting at least one session of resistance training for a week), MFI (muscle fatigue index); $p < .05$. ** $p < .01$. *** $p < .001$.

B = Unstandardized regression coefficient; β = Standardized regression coefficient

FIGURES

Figure 1. Comparing mean MFI (muscle fatigue index) by menopausal status. Values are mean $\pm$ SE.

APPENDICES

APPENDIX A. Women's Health Improvement Initiative screening questionnaire

Thank you for your interest in our research study.

The purpose of this research study is to assess markers of physical and mental health and quality of life among middle-aged women. We are asking eligible participants to come to the Department of Kinesiology at the University of Rhode Island for two measurement visits that will be completed 7-10 days apart. If you participate in the study, we will measure your body composition, ask you questions about yourself, such as questions about your body perceptions, personality, and well-being, assess your physical function, muscular strength, and assess your levels of physical activity and levels of stress. We will also ask you to wear a physical activity monitor clipped to your waist during all waking hours for 7 days, provide us with saliva samples and answer some questionnaires at home during the time between your visits.

Do you think you might be interested in participating in this study?

- ☐ Yes
☐ No

Before enrolling you in our study, we need to ask you some questions to determine if you are eligible. Please answer the following questions about yourself and your health history. This should only take about 15 minutes of your time. Some of these questions pertain to sensitive topics and therefore there is a possibility that some of these questions may make you uncomfortable. If so, you can skip any questions you do not choose to answer.

All information that you share in this screening process, including your name and any other information that can possibly identify you, will be strictly confidential and will be kept under lock and key. If after completion of this screening process it is determined that you are not eligible for the study then, if you grant us permission, we will keep your screening information in a password protected computer file in the event our eligibility criteria change and you then become eligible for participation in the current study.

If you do not want us to keep your information on file, we will record the reason for your ineligibility, without any of your identifying information and then destroy your screening information. If you are eligible for the study and you decide to participate, your information will be coded with an identifying number and we will contact you to schedule your first visit. Remember, your participation is voluntary; you can refuse to answer any questions or stop the screening process at any time without penalty or loss of benefits to which you are otherwise entitled.

Do we have your permission to ask you these questions?

- ☐ Yes
☐ No

This study includes the administration of bone and body composition scan, using Dual Energy X-ray Absorptiometry, commonly referred to as a DXA scan or a bone scan. This scan uses a small amount of radiation to assess your body composition including your fat mass, muscle mass and bone density. The three scans that we are administering together amount to approximately 1/6 of the amount of radiation used during one traditional x-ray.

Are you willing to undergo a DXA scan?

- ☐ Yes
☐ No

Are you between the ages of 40 and 64 years?

- ☐ Yes
☐ No

What is your date of birth?

	Please enter below
Month	<input type="text"/>
Date	<input type="text"/>
Year	<input type="text"/>

What is your current age in years?

Do you understand spoken and written English?

☐ Yes

☐ No

What is your current height in feet and inches?

Feet

Inches

What is your current weight in pounds?

What is your highest weight in the past 3 months in pounds?

What is your lowest weight in the past 3 months in pounds?

Do you live independently?

☐ Yes

☐ No

Are you able to transport yourself or obtain transportation to the URI Kingston campus for 2 measurement visits?

- ☐ Yes
☐ No

Do you currently smoke or have you smoked within the past 6 months?

- ☐ Yes
☐ No

Have you recently experienced a cardiovascular disease event (e.g. recent myocardial infarction, stent placement) or do you have unstable cardiovascular disease (e.g. unstable angina)?

- ☐ Yes
☐ No

Do you have a history of COPD (e.g. chronic bronchitis, emphysema) or severe asthma?

- ☐ Yes
☐ No

Do you have a history of severe orthopedic/musculoskeletal or neuromuscular impairments that would contraindicate exercise (including severe arthritis)?

- ☐ Yes
☐ No

If you answered yes above, please provide us with some information about these conditions:

Have you been diagnosed with Type 1 or Type 2 Diabetes mellitus?

- ☐ Yes
- ☐ No

Have you been diagnosed with Type 1 or Type 2 Diabetes mellitus?

- ☐ Type 1
- ☐ Type 2

Is your medication stabilized?

Have you been diagnosed with HIV?

- ☐ Yes
- ☐ No

Do you have a history of dizziness or balance disorders?

- ☐ Yes
- ☐ No

Have you ever been diagnosed with mental illness, clinical depression or dementia?

☐ Yes

☐ No

If yes, can you tell us more about your diagnosis and treatment plan:

Do you use an assistive device to help you walk (e.g. canes, crutches, walkers, braces)?

☐ Yes

☐ No

Have you ever been diagnosed with any of the following?

	Yes	No
High blood pressure (hypertension)?	☐	☐
High blood cholesterol?	☐	☐
Cardiovascular disease (such as heart disease; heart attack, myocardial infarction), congestive heart failure (CHF), heart rhythm disorders (arrhythmias), heart murmur, chest pain (angina)?	☐	☐
Cerebrovascular disease (such as a stroke, transient ischemic attack (TIA))?	☐	☐
Peripheral Vascular Disease (PVD)?	☐	☐
Chronic Obstructive Pulmonary Disease (such as emphysema, chronic bronchitis)?	☐	☐
Asthma?	☐	☐
Arthritis (such as osteo-arthritis, degenerative joint disease, rheumatoid arthritis)?	☐	☐
Upper gastrointestinal disease (such as an ulcer, hiatal hernia, gastroesophageal reflux disease (GERD))?	☐	☐
Chronic liver disease (such as chronic or persistent hepatitis, cirrhosis)?	☐	☐
Cancer?	☐	☐
a) If yes, please specify type:	☐	☐
<input type="text"/>		
b) If yes, please specify date of diagnosis:	☐	☐
<input type="text"/>		
Anorexia nervosa (not eating and losing extreme amounts of weight)?	☐	☐
Bulimia (eating, sometimes large amounts of food and then vomiting)?	☐	☐
Degenerative disc disease?	☐	☐
Depression?	☐	☐
Anxiety?	☐	☐
Visual impairment (such as cataracts, glaucoma, macular degeneration)?	☐	☐

Hearing impairment?	☐	☐
Thyroid dysfunction (such as hyperthyroidism, hypothyroidism)?	☐	☐
Fibromyalgia?	☐	☐
Chronic fatigue syndrome?	☐	☐
Anemia?	☐	☐
Hashimoto's disease?	☐	☐
Epilepsy?	☐	☐
Lupus (SLE)?	☐	☐
Endometriosis?	☐	☐
Moderate to severe back pain?	☐	☐
Frequent and/or severe headaches?	☐	☐
Environmental allergies?	☐	☐
Do you have a history of having broken bones?	☐	☐
Have you had any surgeries as an adult?	☐	☐
a) If yes, please provide information about the nature of the surgery below.	☐	☐
<div style="border: 1px solid black; height: 20px; width: 150px;"></div>		

Do you have any other health issues you would like to disclose?

- ☐ Yes
- ☐ No

If yes, please provide information in the space below.

Do you take any medications or supplements?

☐ Yes

☐ No

If yes, please list these in the space below, and indicate the dose (amount) you take, what you take the medication to treat, and the frequency with which you take this medication.

Which of the following racial or ethnic groups best describes you? (Please select all categories that apply.)

☐ Asian/Pacific

☐ Black

☐ Hispanic

☐ Indian/Alaskan

☐ White

☐ Other: Please describe

How many alcoholic beverages do you drink (includes wine, beer and hard liquor)?

- ☐ None
- ☐ Less than once a week
- ☐ 1-3 drinks per week
- ☐ 4-6 drinks per week
- ☐ 1 drink daily
- ☐ 2 drinks daily
- ☐ 3 drinks daily
- ☐ More than 3 drinks daily

How many caffeinated beverages do you drink (includes coffee, soda, energy drinks)?

- ☐ None
- ☐ Less than once a week
- ☐ 1-3 drinks per week
- ☐ 4-6 drinks per week
- ☐ 1 drink daily
- ☐ 2 drinks daily
- ☐ 3 drinks daily
- ☐ More than 3 drinks daily

On average, how many meals do you consume each day?

Do you try to eat a special diet?

☐ Low fat

☐ Low carbohydrate

☐ High protein

☐ Vegetarian

☐ Other:

How many servings of dairy do you consume each day?

How many servings of fruits do you consume each day?

How many servings of vegetables do you consume each day?

How many servings of fish do you consume each week?

Please describe your current employment.

Would you describe your current employment as:

- ☐ Full time – working at least 35 hours/week
- ☐ Part time – working less than 35 hours/week
- ☐ Laid-off or unemployed, but looking for work
- ☐ Laid-off or unemployed, but not looking for work
- ☐ Retired, not working at all
- ☐ Retired, working part-time
- ☐ Disabled
- ☐ Full time homemaker
- ☐ Other, please specify:

If you are retired, please describe your primary occupation when you were working.

Please tell us about your highest level of education:

- ☐ Less than a high school diploma
- ☐ High school diploma or equivalent
- ☐ Some College
- ☐ Graduated from college
- ☐ Graduate or professional degree

Have you ever been married or lived with a partner?

- ☐ Yes
- ☐ No

Have you ever been divorced or had a live-in relationship end?

- ☐ Yes
- ☐ No
-

Have you ever been widowed or had a live-in partner die?

- ☐ Yes
- ☐ No
-

Do you now live with a partner or spouse?

- ☐ Yes
- ☐ No
-

If you currently live with a partner or spouse, what is your partner's highest level of

education (last grade completed or degree(s) received):

- ☐ Less than a high school diploma
- ☐ High school diploma or equivalent
- ☐ Some college
- ☐ Graduated from college
- ☐ Graduate or professional degree

Your total yearly household income (includes income from all sources):

- ☐ \$0-14,999
- ☐ \$15,000-29,999
- ☐ \$30,000-44,999
- ☐ \$45,000-59,999
- ☐ \$60,000-74,999
- ☐ \$75,000-99,999
- ☐ \$100,000-149,999
- ☐ \$150,000-199,999
- ☐ \$200,000-249,999
- ☐ \$Over 250,000

Other than yourself, how many people live in your household?

Do you have children (biological, adopted or extended family)?

- ☐ Yes
- ☐ No

If yes, how many?

How many (if any) currently live with you?

What are the current major stressors or life changes in your life?

Please provide an explanation here:

Any major changes in family health during the past year?

If yes, please explain:

How would you describe your sexual orientation?

☐ Heterosexual

☐ Lesbian

☐ Bisexual

☐ Other (please specify:)

How would you describe your current menstrual status?

☐ Premenopause (before menopause; having regular periods)

☐ Perimenopause/menopause transition (changes in periods, but have not gone 12 months in a row without a period)

☐ Postmenopause (after menopause)

If you are post menopausal, was your menopause:

- ☐ Spontaneous (natural)
- ☐ Surgical (removal of both ovaries)
- ☐ Due to chemotherapy or radiation therapy
- ☐ Other, please explain:
- ☐ Not applicable

If you are no longer having periods, what was your age when you had your last period?

If you are still having periods, how often do they occur?

On average, how many days does your period last?

Are your periods painful?

- ☐ Yes
- ☐ No
- ☐ Not applicable

If yes, how painful?

- ☐ Mild
- ☐ Moderate
- ☐ Severe
- ☐ Not applicable

Do you have any problems with PMS?

- ☐ Yes
- ☐ No

How would you rate your knowledge about menopause?

- ☐ Very good
- ☐ Moderately good
- ☐ Fair
- ☐ Little Knowledge

Where do you get your information about menopause (mark all that apply)

- ☐ Books
- ☐ Internet
- ☐ Magazines
- ☐ Friends
- ☐ TV
- ☐ Health care providers
- ☐ Other

How do you view menopause?

- ☐ Positively. For example, menopause means no more periods and no more worry about contraception.
- ☐ Neutral.
- ☐ Negatively. For example, menopause means a loss of fertility and loss of youth.
- ☐ Other:

What concerns you about menopause? Please provide any of your thoughts in the space provided.

What are your current views regarding hormone therapy for menopause?

- ☐ Positive. Hormone therapy is appropriate for some women.
- ☐ Neutral.
- ☐ Negative. I don't support the use of hormone therapy.

What concerns you most about hormone replacement therapy? Please provide any of your thoughts in the space provided.

Please mark the appropriate box with ☐ to record your response to the following: How often do you engage in each of the following behaviors?

	Every 6 months	Once a year	Every 2 years	More than every 2 years	Never
See a health care professional for a general physical exam?	☐	☐	☐	☐	☐
See a health care professional for a women's health exam?	☐	☐	☐	☐	☐
See a dental professional for a dental exam/cleaning?	☐	☐	☐	☐	☐
See a health care professional for an eye exam?	☐	☐	☐	☐	☐

Please mark the appropriate box to record your response to the following: How often do you engage in each of the following behaviors?

	Every month	Every 6 months	Once a year	Every 2 years	More than every 2 years	Never
How often do you have a pap smear?	☐	☐	☐	☐	☐	☐
How often do you have breast exams by a doctor or nurse?	☐	☐	☐	☐	☐	☐
How often do you have mammograms?	☐	☐	☐	☐	☐	☐
How often do you breast self-examine?	☐	☐	☐	☐	☐	☐

What is the best way to contact you?

☐ Phone

☐ Email

☐ Mail

☐ Other

Please enter the following contact information:

☐ Full Name

Please provide us with a phone number to reach you (including area code)

☐ Phone Number

Please provide us with an email address (if you have one)

☐ Email Address

Please provide us with a mailing address, including Street, City/Town, Zip Code

☐ Address

Thank you very much for your time. Based on the information you provided us in this questionnaire, we will determine your eligibility to participate in the study. We will be contacting you in the near future to schedule your first visit to the research lab at the University of Rhode Island. If you have any questions about this research project, please feel free to contact our Principal Investigator, Dr. Sabik by email at sabik@uri.edu or by phone at (401) 874-5439. You can contact Dr. Ward-Ritacco by email christieward@uri.edu or by phone at (401) 874-5638.

APPENDIX B. Women's Health Improvement Initiative informed consent

HEALTH STUDIES PROGRAM
25 Independence Way, Suite P, Kingston, RI 02881 USA p: 401.874.7499 f: 401.874.4215 web.uri.edu/health-studies

Project Title: Evaluating Physical Function and Self Perception in Middle-Aged Women

CONSENT FORM FOR RESEARCH

You have been invited to take part in the research project described below. A member of the research team will explain the project to you in detail. You should feel free to ask questions. If you have more questions later, Dr. Natalie Sabik and Dr. Christie Ward-Ritacco, the persons mainly responsible for this study, will be happy to talk with you about them. You can contact Dr. Sabik by email at sabik@uri.edu or by phone at (401) 874-5439. You can contact Dr. Ward-Ritacco by email christieward@uri.edu or by phone at (401) 874-5638.

Inclusionary Criteria

To be a candidate for this study you must 1) be able to speak and read English, 2) be a woman, 3) be between 40 - 64 years of age, 4) have no recent changes in your body weight (within ~5 pounds for the past 3 months), 5) have a body mass index of 18.5 – 45.0 kg/m², 6) be a non-smoker, 7) not be pregnant, 8) be willing to have a dual energy X-ray absorptiometry (DXA) scan, 9) be free of diseases or conditions that would prevent reasonably safe participation in study related testing, and 10) be living independently.

Project Description

The main purpose of this study is to assess how physical factors, such as exercise, body composition, and muscular strength, relate to well-being among middle-aged women. We want to learn about how these factors are related because physical changes during midlife place women at increased risk of poorer quality of life, including increased functional limitations and decreased psychological well-being. A growing number of middle-aged Americans are reporting decreases in their physical health, mental health, ability to perform activities of daily living, and ability to work. Examining the associations between these factors will help us to understand barriers to health and will allow us to design effective interventions to improve quality of life in middle-aged women.

Your participation will include coming to the URI Kingston campus for two testing visits and completing a series of tasks at home in between your visits. All of the testing will take place on the URI Kingston campus in Independence Square. You are responsible for your own transportation to all of the testing visits.

Time Commitment

Interested women will complete a short online screening questionnaire. Women who qualify to take part in the research study will be asked to come to the Department of Kinesiology at the University of Rhode Island for two visits that will occur 7-10 days apart. During the time between visits you will complete a series of questionnaires. The total time commitment for this study is 7 hours.

IRB NUMBER: HU1516-206
IRB APPROVAL DATE: October 23, 2017
IRB EXPIRATION DATE: October 19, 2018

What Will I Do As a Participant in This Study?

If you choose to participate in the study you will be asked complete two in person visits and complete a series of tasks at home between the two visits.

Visit 1:

First we will check your interest and ability to take part in this study. Then we will review and sign this form. Next, we will complete a paper and pencil administered questionnaire making sure that you are able to engage in physical activity safely and one to examine your cognitive performance.

Next, a qualified member of the research team will collect 160 microliters (about a half a teaspoon) of your blood using a finger stick technique. Your blood sample will be analyzed for hemoglobin and hematocrit, to assess your risk for anemia.

After your blood sample is taken, we will measure your height and weight, your waist circumference, and take your heart rate and blood pressure. Then you will have a DXA scan in room 129 of the Independence Square building. A DXA scan is a body scan that tells us information about your body fat, your muscle mass, and your bone density. We will provide you with medical “scrubs” to wear during scanning if you are wearing clothing that would interfere with the scan. You will lie on a padded table that remains stationary as the scanning arm moves over your body. Total scanning time, complete with positioning, takes approximately 20 minutes. A licensed radiology technician will perform the DXA scans. There is no cost to you or your insurance for these scans. If you are pre-menopausal (not self-identified as post-menopausal or otherwise unable to become pregnant), you will complete a pregnancy test prior to completing your DXA scan. One will be provided to you with no cost to you or your insurance company. You will provide a small urine sample by peeing in a cup and then provide the sample to the researcher, who will conduct the pregnancy test to confirm that you are not pregnant prior to having the DXA scan.

In addition we will ask you to complete several questionnaires using a computer in our laboratory. The questionnaires will ask you about your quality of life, your feelings of energy and fatigue, your sleep quality, your stress levels, your physical activity history, and will also contain questions about your emotional and physical health and well-being. Next you will complete a series of tasks to measure your physical functional ability. These include sitting in chair and standing up as many times as you can in 30 seconds, standing from seated position and walking around a cone placed in front of you as quickly as possible, lifting a weighted crate and carrying it through a marked course, getting up and off the floor as quickly as possible, and walking for 6 minutes as quickly as you can. During the functional assessments we will ask you to rate your feelings of effort, fatigue, and pain. You can rest between each activity. Any risk of injury during the completion of these tasks will be minimized by having all sessions supervised by a research team member qualified to direct this type of testing.

Before you leave for the day, we will review how to wear your physical activity monitoring device for 7-10 days while you go about your normal daily routine. We will ask you to wear your physical activity monitor during all waking hours except when showering or swimming. We will also show you how to fill out your physical activity log. This will require you to write down the type of activity, the time of the activity, and how many minutes you completed of during each bout of planned, structured physical activity (e.g. 30 minutes of walking outside at 3:30 pm). We will also review how to provide saliva samples and review the questionnaires that you will be asked to fill out at home in the time between visits 1 and 2.

THE
UNIVERSITY
OF RHODE ISLAND
OFFICE OF RESEARCH
AND INNOVATION
PROTECTORATE

IRB NUMBER: HU1516-206
IRB APPROVAL DATE: October 23, 2017
IRB EXPIRATION DATE: October 19, 2018

In between Visits 1 and 2:

You will be asked to complete a series of questionnaires asking you about your physical activity history, your menopausal symptoms, how you feel about your body and age, social activities, and your daily feelings of energy at home. If you would like to complete these on your home computer, we will email a link to you from Qualtrics, an online survey tool, containing the questionnaires. If however, you would prefer to answer offline or do not have access to a computer, we will provide you with hard copies of all of the questionnaires. You will wear your physical activity monitor and record any planned physical activity/exercise sessions on your physical activity log. You will bring your completed physical activity log, your physical activity monitor, and completed questionnaires (if applicable) to the lab when you return for Visit 2. You will also be asked to provide us with 10 saliva samples total (5 per day for 2 days). The saliva sample will provide us with information about how your body responds to stress. To create these samples you will simply chew on a cotton swab provided by the researchers and will spit it into a tube to be stored in the refrigerator. You will be asked to bring these with you to the lab on Visit 2.

Visit 2:

At Visit 2, we will collect your physical activity monitor and check and collect your physical activity log. If there are any missing information on your physical activity log we will ask you to try and fill it in as best as you can remember. We will also collect your saliva samples. We will also ask you to complete any unfinished questionnaires in our laboratory. When this is finished, we will test your hand grip strength by squeezing the lever on a small hand-held device, known as a hand grip dynamometer. This task is repeated three times with both the right and left hands. We will then test the strength of your upper leg. This involves being seated in a special machine that controls the speed with which you can move your leg and measures how much force you are able to produce while you kick and pull with your knee. Then we will check your muscular endurance. During each task you will receive real-time visual feedback on a computer monitor and verbal encouragement to help you. During the strength and endurance tests we will ask you to rate your feelings of effort, fatigue and pain. You can rest between each exercise.

Risks or Discomfort

It is possible that heart or blood vessel problems could arise during your participation in the study testing. Although highly unusual, it is possible that these problems could lead to a heart attack, stroke or even death. It is possible that these risks will not be eliminated completely, even with a medical evaluation prior to participation in the study. However, the investigators believe the risk of harm from study participation is relatively small and that the benefits of the study to you individually will likely outweigh any potential risks. You may experience some temporary muscle soreness as a result of the testing sessions. There is also a risk skeletal injury from testing. The investigators will use procedures designed to minimize this risk. Because some of the physical function tasks require some degree of balance, there is a risk of falling associated with completing these tasks. However, the investigators will take precautions to reduce the chance of falling. There is a risk of bruising, pain, and in rare cases, infection or fainting as a result of finger stick blood sampling. However, these risks to you will be minimized by allowing only qualified people to use the finger stick technique to take a small sample of your blood.

You understand that there will also be a very low total radiation dose for the DXA scans (~9 millirem), which is well below the maximal annual radiation dose (5 rems) allowed for exposure

IRB NUMBER: HU1516-206
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in the workplace. Naturally occurring radiation (cosmic radiation, radon gas, etc.) gives each person a whole body radiation dose of about 300 millirems per year. Therefore, the total dose of radiation exposure from DXA is considered low. The major risk from high radiation exposure is passing on damaged genes (genetic mutations) to offspring. Therefore, this risk is of primarily a concern for women who are of childbearing age.

In case there is any injury to the subject:

In the event of physical injury resulting from participation in this study, upon your consent, emergency treatment will be available at South County Hospital with the understanding that any injury requiring medical attention becomes your financial responsibility. URI will not provide any medical or hospitalization insurance coverage for participants in this research study, nor will they provide compensation for any injury sustained as a result of this research study, except as required by law.

Benefits of this study:

This study may help the investigators better understand which factors are most important in determining quality of life in middle-aged women. The results of this study may be used in the future to design effective interventions for improving physical and psychological health in middle-aged women. Additionally, as a participant in this study you will be provided with the results of your hemoglobin and hematocrit testing, a copy of your DXA scan, and the results of your muscular strength and physical function testing.

Participant Compensation:

For your participation in the study and after the study is completed, you will receive, free of charge, information about your blood test results, body composition, muscle strength, and physical function. Participants will be compensated \$100 total in the form of gift cards upon completion of all study requirements. For participants that withdraw from the study early, compensation will be prorated based on the time spent completing study materials. Pro-rating will occur as follows: for completion of the initial laboratory visit, you will receive \$30. For completion of at-home activities (questionnaires, wearing and returning accelerometer, collecting saliva samples) and visit 2, participants will receive \$70. For participants that withdraw early from the study, study equipment must be returned to receive payment.

Confidentiality:

All information collected in this study is confidential, and your name will not be identified and linked to any electronic study data at any time to anyone other than the principal investigators of the study. Your data will be coded with an ID number only, which will be linked back to you only by the principal investigators of the study. Your part in this study is confidential within legal limits. The researchers and the University of Rhode Island will protect your privacy, unless they are required by law to report information to city, state or federal authorities, or to give information to a court of law. Otherwise, none of the information will identify you by name

All study data, including this consent form, will be locked in a file cabinet and also stored in a study computer with a password secured in our locked study office (Independence Square building, Suite P, room 225). All study data will be kept for three years after study completion.

IRB NUMBER: HU1516-206
IRB APPROVAL DATE: October 23, 2017
IRB EXPIRATION DATE: October 19, 2018

Decision to Quit at any Time:

It is your decision alone whether or not you participate in this study. You are free to ask questions about this study before you decide whether or not to participate. Also, if you consent to participate in the study you are free to quit at any time without penalty, or without any requirement that you provide an explanation about your decision to withdraw.

Rights and Complaints:

If you are not happy with the way this study was done, you may talk with Dr. Natalie Sabik or Dr. Christie Ward-Ritacco. They can be reached at (401) 874-5439 or (401) 874-5638, respectively. You can talk to either of them anonymously if you want to. In addition, if this study causes you any injury or if you have questions about your rights as a research subject you may contact the office of the Vice President for the Division of Research and Economic Development, Carlotti Administration Building, 2nd Floor, 75 Lower College Road, Suite 2, University of Rhode Island, Kingston, Rhode Island; telephone: (401) 874-4576.

Further, we would like to know if we can retain your contact information to potentially contact you to provide the opportunity to participate in future research. You can choose to participate in the current study and can opt to not be contacted in the future.

I would like to provide my contact information to be contact for future research studies.

☐ Yes Phone: _____

☐ No Email: _____

You have read and understand the above information in the Consent Form and have been given adequate opportunity to ask the investigators any questions you have about the study. Your questions, if any, have been answered by the investigators to your satisfaction. Your signature on this form means that you understand the information and you agree to voluntarily participate in this study.

Signature of Participant	Date	Signature of Researcher	Date
Typed/printed Name		Typed/printed name	

Please sign both consent forms, the research team will keep one copy and you will be given one for yourself.

IRB NUMBER: HU1516-206
IRB APPROVAL DATE: October 23, 2017
IRB EXPIRATION DATE: October 19, 2018

APPENDIX C. Physical Activity Readiness Questionnaire (PAR-Q)

Physical Activity Readiness
Questionnaire - PAR-Q
(revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO	
☐	☐	1. Has your doctor ever said that you have a heart condition <u>and</u> that you should only do physical activity recommended by a doctor?
☐	☐	2. Do you feel pain in your chest when you do physical activity?
☐	☐	3. In the past month, have you had chest pain when you were not doing physical activity?
☐	☐	4. Do you lose your balance because of dizziness or do you ever lose consciousness?
☐	☐	5. Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?
☐	☐	6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?
☐	☐	7. Do you know of <u>any other reason</u> why you should not do physical activity?

If
you
answered

YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active — begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal — this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

DELAY BECOMING MUCH MORE ACTIVE:

- if you are not feeling well because of a temporary illness such as a cold or a fever — wait until you feel better; or
- if you are or may be pregnant — talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Informed Use of the PAR-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

NAME _____

SIGNATURE _____

SIGNATURE OF PARENT
or GUARDIAN (for participants under the age of majority) _____

DATE _____

WITNESS _____

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.

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APPENDIX D. Mini-Mental State Examination

Mini-Mental State Examination (MMSE)

Patient's Name: _____

Date: _____

Instructions: Ask the questions in the order listed. Score one point for each correct response within each question or activity.

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day of the week? Month?"
5		"Where are we now: State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible. Number of trials: _____
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, ...) Stop after five answers. Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.)
30		TOTAL

(Adapted from Rovner & Folstein, 1987)

Instructions for administration and scoring of the MMSE

Orientation (10 points):

- Ask for the date. Then specifically ask for parts omitted (e.g., "Can you also tell me what season it is?"). One point for each correct answer.
- Ask in turn, "Can you tell me the name of this hospital (town, county, etc.)?" One point for each correct answer.

Registration (3 points):

- Say the names of three unrelated objects clearly and slowly, allowing approximately one second for each. After you have said all three, ask the patient to repeat them. The number of objects the patient names correctly upon the first repetition determines the score (0-3). If the patient does not repeat all three objects the first time, continue saying the names until the patient is able to repeat all three items, up to six trials. Record the number of trials it takes for the patient to learn the words. If the patient does not eventually learn all three, recall cannot be meaningfully tested.
- After completing this task, tell the patient, "Try to remember the words, as I will ask for them in a little while."

Attention and Calculation (5 points):

- Ask the patient to begin with 100 and count backward by sevens. Stop after five subtractions (93, 86, 79, 72, 65). Score the total number of correct answers.
- If the patient cannot or will not perform the subtraction task, ask the patient to spell the word "world" backwards. The score is the number of letters in correct order (e.g., dlrow=5, dlrow=3).

Recall (3 points):

- Ask the patient if he or she can recall the three words you previously asked him or her to remember. Score the total number of correct answers (0-3).

Language and Praxis (9 points):

- Naming: Show the patient a wrist watch and ask the patient what it is. Repeat with a pencil. Score one point for each correct naming (0-2).
- Repetition: Ask the patient to repeat the sentence after you ("No ifs, ands, or buts."). Allow only one trial. Score 0 or 1.
- 3-Stage Command: Give the patient a piece of blank paper and say, "Take this paper in your right hand, fold it in half, and put it on the floor." Score one point for each part of the command correctly executed.
- Reading: On a blank piece of paper print the sentence, "Close your eyes," in letters large enough for the patient to see clearly. Ask the patient to read the sentence and do what it says. Score one point only if the patient actually closes his or her eyes. This is not a test of memory, so you may prompt the patient to "do what it says" after the patient reads the sentence.
- Writing: Give the patient a blank piece of paper and ask him or her to write a sentence for you. Do not dictate a sentence; it should be written spontaneously. The sentence must contain a subject and a verb and make sense. Correct grammar and punctuation are not necessary.
- Copying: Show the patient the picture of two intersecting pentagons and ask the patient to copy the figure exactly as it is. All ten angles must be present and two must intersect to score one point. Ignore tremor and rotation.

(Folstein, Folstein & McHugh, 1975)

APPENDIX E. Actigraph Accelerometer Instructions

ActiGraph Accelerometer Instructions

Thank you for participating in our study!

What is an accelerometer?

This activity meter records general movement and will allow us to get a better idea of your overall activity level. This device will measure the physical activity you perform by detecting the movements that are made as well as the acceleration of those movements, but will not be able to tell us exactly what activity you are doing. It is easy to use and can be worn on your belt or on the waist band of your clothing. It may feel slightly awkward at first, but after a few hours you will barely know it's there. They are also quite pricey, so please be careful!

Instructions:

You will be given an accelerometer at your study visit by your assigned number. Please do **NOT** switch accelerometers with anyone!

Please wear the ActiGraph with the belt clip fastened around the waist with the unit positioned over the **right** hip bone.

You can wear your activity monitor over or under clothing, whichever is most comfortable to you! The meter does not need to be in direct contact with the body. However, it is essential that the ActiGraph be positioned snugly enough against the body that it cannot flop around.

If you take it off for any reason, please write that on your tracking log. You will keep track of the time the accelerometer was worn using the Accelerometer Log form.

Please do not wear this device in any other way, including:

- NOT in any pockets of clothing
- NOT in a backpack or handbag
- NOT in a car glove compartment or trunk

During the week-long wear period, you will be given the accelerometer at your first visit. You will wear it during the visit and for the rest of the day. For the rest of the week it will be worn during all waking hours until you return it at your second study visit.

APPENDIX F. Actigraph Accelerometer Record of Wear

Accelerometer Record of Wear

Subject ID: _____

Week: _____

PRE

POST

Day of the week	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Date (month/day)	____/____	____/____	____/____	____/____	____/____	____/____	____/____
Time On	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
Time Off	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
If the monitor was removed during waking hours, list the times and reasons for each removal:							
1. Time Took Off:	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
1. Reason Took Off:							
1. Time Back On:	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
2. Time Took Off:	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
2. Reason Took Off:							
2. Time Back On:	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
List any exercise you performed while NOT wearing the monitor (e.g., walking, jogging, swimming, cycling, aerobics):							
1. Exercise Type:							
1. Exercise Start:	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
1. Exercise Stop:	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
2. Exercise Type:							
2. Exercise Start:	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
2. Exercise Stop:	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
Walking Diary: List any brisk walks you took that were at least 10 minutes long:							
Walk 1 Start Time:	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
Walk 1 Stop Time:	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
Walk 2 Start Time:	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM
Walk 2 Stop Time:	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM	____ : ____ AM or PM

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