HOW PAIN EXPEDITES THE AGING PROCESS:

IMPROVING OUR UNDERSTANDING OF DISABILITY DEVELOPMENT IN OLDER ADULTS WITH CHRONIC LOW BACK AND RADICULAR LEG PAIN

by

Peter Charles Coyle

A dissertation submitted to the Faculty of the University of Delaware in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Biomechanics and Movement Science

Spring 2017

HOW PAIN EXPEDITES THE AGING PROCESS:

IMPROVING OUR UNDERSTANDING OF DISABILITY DEVELOPMENT IN OLDER ADULTS WITH CHRONIC LOW BACK AND RADICULAR LEG PAIN

by

Peter Charles Coyle

Approved: _____

Samuel Lee, Ph.D.
Director of the Biomechanics and Movement Science Program

Approved: _____

Kathleen S. Matt, Ph.D.
Dean of the College of Health Sciences

Approved: _____

Ann L. Ardis, Ph.D.
Senior Vice Provost for Graduate and Professional Education

I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed: _____

Gregory E. Hicks, Ph.D.
Professor in charge of dissertation

I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed: _____

Jennifer Schrack, Ph.D.
Member of dissertation committee

I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed: _____

Darcy Reisman, Ph.D.
Member of dissertation committee

I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed: _____

William Farquhar, Ph.D.
Member of dissertation committee

I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed: _____

Jaclyn M. Sions, Ph.D.
Member of dissertation committee

I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed: _____

Ryan Pohlig, Ph.D.
Member of dissertation committee

ACKNOWLEDGMENTS

There are not enough words in the English language, let alone space in this document, to express the level of gratitude that I feel for the people who made this project possible. First, I would like to thank my dissertation committee members for their guidance and support. Bill, your expertise in exercise physiology was critical to the life of this project. Darcy, your experience with the nature of this work, and your ability to make me think about my research questions from a different perspective, were invaluable. Ryan, without your help, I would still be running these analyses; thank you for your flexibility and patience. Meg, you have worked tirelessly to make sure that we, as a lab and as individuals, are successful; I can never truly express how much I appreciate that. Jennifer, your work was the inspiration for the genesis of this project; thank you for dedicating your time and energy in bringing life to it. Finally, Greg, it is impossible to sum up in one sentence, the contributions that you have made to this project, my career, and my development as an adult; you are simply one of the greatest teachers under whom I have ever had the pleasure to study.

Second, I would like to acknowledge my colleagues, starting with the members of the Delaware Spine Studies team. Teonette, Tori, and Jeni, you have made coming into work enjoyable. To the research and clinical faculty in the UDPT department, your support, patience, and dedication towards making me a better researcher, clinician, and person, has always been noticed and appreciated. To my fellow PhD students throughout the years, thank you for your kindness and support.

Third, I would like to thank my support network. Jeni, Alex, and Anthony, I cannot express how grateful I am to be a part of your family; you are the epitome goodness. Jeni, I also have to express my gratitude to you, personally, for your support and guidance throughout this process; you are a great writer, an excellent teacher, and an even better friend. Anthony, Dana, and Matt, thank you all for your love, support, and patience. Matt, I would like to express my thanks for your direct contributions to this project; I would still be writing computer code had it not been for you. Cait, thank you for your love and support over this past year; I look forward to seeing where life takes us. I would like to thank my family: Mom, Dad, Memom, Grandmom, Dennis, Nicole, and Chris. I love you all more than life itself, and I am proud to call myself your son, grandson, and brother; you have made me into the man that I am today, and that's not too shabby.

Finally, I would like to acknowledge the organizations and institutions who have made my PhD training possible. The National Institutes of Health have provided me with financial support to complete my work. These grants include the University of Delaware's T32HD007490 from the Eunice Kennedy Shrive National Institute of Child Health & Human Development; Dr. Hicks' R21HD057275 and R01AG0412202 from the National Institute on Aging; and, the Adopt-A-Doc Award from the APTA's Academy of Geriatric Physical Therapy. Last, I would like to acknowledge the researchers at the Baltimore Longitudinal Studies of Aging, who provided me with the data and guidance to complete a major component of this project.

Again, thank you *all* for your contributions to this project and my career.

DEDICATION

This project is dedicated to Richard J. Coyle and Richard E. LeCates.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Background: Chronic musculoskeletal pain is prevalent, costly, and disabling among older adults. Decreases in walking speed are a hallmark sign of the age-related deterioration of mobility, and are more pronounced among those with chronic musculoskeletal pain. Walking speed is strongly predictive of adverse health outcomes, such as institutionalization and mortality. Although we are unsure *why* this occurs, recent evidence suggests that the age-related decline in walking speed may be due, in large part, to impaired energetic efficiency and energetic capacity. The combination of pain in the presence of age may have an important impact on this metabolic pathway. Rehabilitation interventions targeted at points along this pathway may improve pain-related disability.

Purpose: We aim to: 1) propose a new conceptual framework to enhance the understanding of the energetic mechanisms behind the deterioration of mobility among older adults with pain; 2) test different aspects of this model using different patient populations and study designs; 3) provide insight as to the clinical implications that this new model possesses.

Methods: Hypotheses will be investigated using two different study designs. First, the energetic efficiency and energetic capacity of older adults with chronic low back and radicular leg pain will be explored; this patient population offers a unique insight into the relationship between pain and energy expenditure, because their symptoms are provoked with walking. Second, we will conduct a secondary analysis of a longitudinal dataset to examine the potential predictive relationship that energy

efficiency has on energetic capacity, and to investigate the influence that lumbopelvic pain has on this relationship, among older adults.

Significance: Validation of this conceptual model will have important clinical implications. If energetic efficiency and energetic capacity are impacted by the presence and provocation of chronically painful conditions, then they will be important clinical targets for rehabilitation. Our findings lend support to this model. Provocation and the mere presence of chronic low back and radicular leg pain are linked to worse energetic efficiency and capacity. Longitudinally, energetic efficiency is predictive of changes in energetic capacity, and this relationship may be moderated by the presence of severe lumbopelvic pain.

Chapter 1

THE PAIN-ENERGY MODEL OF MOBILITY LIMITATION

1.1 Introduction

The International Association for the Study of Pain defines pain as, "an unpleasant sensory and emotional experience associated with actual or potential damage, or described in terms of such damage."[1] Pain is a multifactorial, complex process that places a massive burden on society. Experts estimate that chronic pain conditions account for over $600 billion annually in direct and indirect health care costs.[2] The prevalence of chronic pain rises with age, primarily due to the development of musculoskeletal conditions and neurodegenerative processes.[3] Furthermore, pain-related health care costs continue to rise in the aging population.[4] Medicare claims data from 1991-2002 reveal a 300% increase in charges related to low back pain,[4] a common chronic condition among older adults.[5] In addition, older adults with chronic pain are at a higher risk for disability and a reduced quality of life.[6-10]

Decreases in walking speed, which are a hallmark sign of the disablement process,[11,12] are commonly seen among older adults with chronically painful conditions (e.g. symptomatic knee osteoarthritis and chronic low back pain). Walking is arguably the most important aspect of functional mobility, as walking speed alone is a strong predictor of adverse outcomes, such as disability[12-14] and mortality.[15] Current evidence suggests that older adults with chronic pain walk slower than their pain-free peers[7,10,16-20]; however, the primary drivers of this deterioration in mobility remain

unclear. To develop effective interventions, we must first have a better understanding of the mechanisms through which disability develops in these geriatric patient populations.

Among older adults with pain, there are many conceivable pathways through which limitations in mobility may occur. Perhaps the most commonly held belief is that some individuals with pain avoid certain activities for fear of pain or injury (i.e. fear-avoidant behavior).[21] Theoretically, as people become more fearful of exacerbating their pain, they engage in less physical activity, resulting in physical deconditioning and a perpetuation of the pain and disability cycle.[21,22] Indeed, physical deconditioning has been linked to increased risk of disability[23,24] and death,[25,26] regardless of the presence of pain. Yet fear-avoidance models largely ignore the physiological underpinning of pain that may contribute to this process, instead focusing heavily on the psychosocial factors of pain, which may be highly subjective and variable between individuals. A new model that explores the impact of pain on physiological processes, such as energy metabolism, could generate new research that would enhance our understanding of how painful conditions lead to functional mobility deficits among older adults.

In 2010, Schrack et al proposed a convincing conceptual framework, known as the Energetic Pathway of Mobility Loss, to explain the potential physiological mechanisms behind age-related walking speed decline (i.e. functional mobility decline).[27-29] Pain may play an important role in this process, but its role has not been investigated beyond the broad categorization of “lower extremity arthritis pain.”

1.2 Aging and Energetics

In the Energetic Pathway of Mobility Loss framework, Schrack et al explain how mobility limitations may be the result of age-related changes in the following energy constructs:

1. Energy capacity: the upper limit of energy expenditure per minute available to perform vigorous activities. Often, this is measured by maximal or peak oxygen consumption during sustained, vigorous activity (VO2 max or VO2 peak, respectively).[27]

2. Energy cost of mobility: the energy cost of walking and other mobility-related tasks (e.g. sit-to-stand transitions, stair climbing, etc). Energy expenditure is commonly measured by analyzing the amount of oxygen one consumes during aerobic activity. Because walking is a good surrogate measure for functional mobility,[12,15] this construct is measured by quantifying the amount of oxygen consumed during walking at a fixed, slow pace or at self-selected pace. If measured at self-selected pace, oxygen consumption is often standardized to walking speed to give walking economy (i.e. the energy required to walk one meter).[30]

In general, the Energetic Pathway to Mobility Loss framework can be summarized in three simple premises, which are illustrated in Figure 1.1

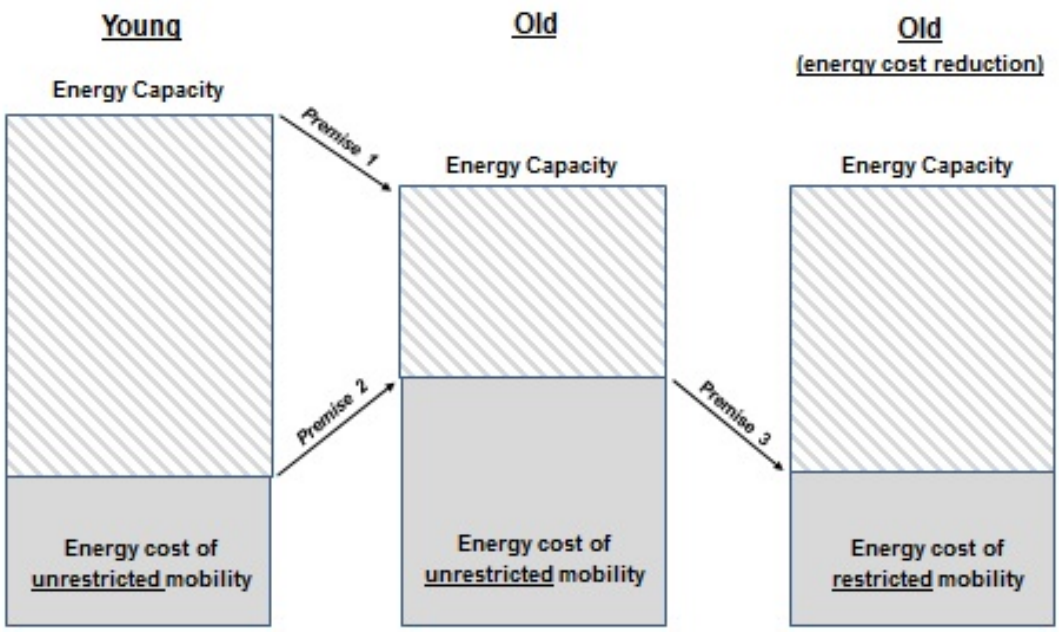

Figure 1.1: Illustration of the Energetic Pathway of Mobility by Schrack et al with premises noted. With age: 1) energy capacity declines, while 2) the energy cost of unrestricted mobility increases. Mobility limitations occur when the energy cost of unrestricted mobility approaches the maximum level of energy a person is capable of expending (i.e. energy capacity). Mobility restrictions are a compensatory strategy for the age-related increase in the energy cost of unrestricted mobility.

Schrack et al propose that, with age, (Premise 1) energy capacity decreases, (Premise 2) the energy cost of mobility increases, and (Premise 3) mobility limitations develop when the energy cost of mobility approaches the maximum level of energy that a person is capable of expending (i.e. energy capacity).[27-29] In the following sections, supporting literature is reviewed for each premise.

Premise 1: Energy capacity decreases with age. Oxygen consumption is an indirect measure of energy expenditure, known as indirect calorimetry, and it is quantified as the amount of oxygen consumed in milliliters per kilogram of

bodyweight per minute (ml/kg/min). Maximal oxygen consumption, the upper limit of energy available to perform vigorous activities, is often measured as VO2 max or VO2 peak. VO2 max begins to decline during the third decade of life, and exponentially deteriorates with each passing decade.[31] For example, previous research suggests that between ages 30 and 39, VO2 peak (a surrogate measure for VO2 max) declines an average of 0.9 ml/kg/min, whereas between ages 60 and 69 years this decline is accelerated, averaging 6.6 ml/kg/min.[31] This non-linear trend continues well into older age, with a reduction in VO2 max values of 12-16 ml/kg/min occurring between the ages of 80-90 years old.[32] Experts have hypothesized that once VO2 max falls below a certain threshold (approximately 18 ml/kg/min), functional limitations are more likely to occur.[23]

Age-related changes in the musculoskeletal system, as well as in the central and peripheral cardiovascular system, combine to contribute to reduced energy capacity.[31,33,34] Sarcopenia, the reduction in lean body mass with age, can contribute to the age-related deterioration of VO2 max.[31] Furthermore, reductions in heart and blood vessel function have been shown to be closely related to declines in VO2 max.[31] With age, stroke volume (i.e. the amount of blood ejected from the heart during each beat) decreases,[31,35] and the ability for oxygen to perfuse through the capillary vessel walls is attenuated.[31] The combined effect of these physiological impairments drive the age-related decline of energy capacity.[31,33,35]

Premise 2: The energy cost of mobility increases with age (i.e. energy inefficiency). Walking is an essential aspect of most daily activities; thus, it serves as a good marker of functional mobility. Walking becomes less efficient with age.[34] Schrack et al have shown that, regardless of age, people will naturally select a walking

speed with an energy cost of approximately 13.0 ml/kg/min; for older adults, the walking speed needed to achieve this rate is much slower than that of younger and middle aged adults,[28] highlighting the age-related changes in energetic efficiency. It is important to note that increases in energy cost of activities are not limited to only walking; Knaggs et al found that the energy cost of a number of daily activities increase with age, when the speed at which each is performed is taken into account.[36]

The mechanisms by which age leads to energy inefficiencies are less clear and may be person-dependent. One mechanism that has been postulated is the age-related increase in chronic disease burden. Chronic disease can cause homeostatic imbalance, which can result in higher levels of resting energy expenditure in order to maintain homeostasis.[37,38] Furthermore, age-related changes in gait mechanics have an impact on energy expenditure, as the severity of gait impairments has been shown to be directly related to the level of energy cost that walking requires among older adults.[39] As one ages, variability in gait mechanics becomes more prominent, resulting in more frequent and larger deviations from optimal biomechanics[40]; these additional movements may be extraneous to the task of walking, increasing the overall energy cost,[41] and thereby resulting in energy inefficiency.

Premise 3: Mobility limitations develop when the energy cost of mobility approaches energy capacity. The age-related decline in the quantity and speed of movement is not a human-specific phenomenon, but rather a core physiologic strategy that is universal across species.[27] For example, Carter et al found that rats walk slower as they age, and slower walking rats have a higher risk of mortality.[42] As noted above, energy capacity declines with age.[31] Consistently performing near the maximal level of energy capacity is dangerous to sustaining life, because of the risk of homeostatic

collapse.[43] Priede et al demonstrated that when fish swim at near maximal energy capacity, they have a higher risk of mortality.[44] As a strategy, animals will decrease their quantity and speed of movement near the end of life (i.e. advanced age),[42,45] presumably when the energy capacity to perform activities is low, and the energy cost of movement is high.

This theory is also consistent with findings in humans. Recently, experts have hypothesized that low energy capacity and high energy cost of mobility work in tandem with one another to yield mobility limitations. Schrack et al have shown that higher energy cost of walking is predictive of walking speed decline in older adults, but not in middle-aged and younger adults.[46] This indicates that higher energy cost of activities are important in the deterioration of mobility, but only in the presence of low energy capacity. In support, prior work in middle aged and older adults has shown that the energy cost of walking is strongly related to mobility levels, but only when energy capacity falls below a certain threshold (approximately 18 ml/kg/min).[29] Taken together, these findings suggest that limitations in mobility, such as decreased walking speed, are more likely to occur when the energy cost of mobility approximates energy capacity.

1.3 Pain-Energy Model: A Novel Conceptual Approach

The findings that older adults with chronic musculoskeletal pain conditions walk slower[7,10,16,18,20] and experience greater reductions in walking speed over time, compared to those without pain,[17,19] support the notion that these conditions expedite the age-related decline of functional mobility. In our physiological framework, the Pain-Energy Model, we hypothesize that the following factors are important in the acceleration of mobility decline among older adults with painful conditions:

1. Pain experience: an unpleasant sensory and emotional experience associated with actual or potential damage, or described in terms of damage.[1] Pain can arise from injury or insult to tissues, which can result in unpleasant sensations. These sensations can be augmented by psychological (e.g. anxiety, fear, etc) and social (e.g. rejection, attachment, etc) factors resulting in not only emotional distress, but also in neurobiological changes.[47]

2. Energy cost of mobility: previously defined (Energetic Pathway of Mobility Loss Energy Constructs).

3. Daily physical activity: The World Health Organization defines physical activity as any bodily movement produced by skeletal muscles that requires energy expenditure.[48] Physical inactivity has been linked to a host of adverse health outcomes, including mortality.[49] Physical activity has been measured through self-report questionnaires and step activity monitors.

4. Energy capacity: previously defined (Energetic Pathway of Mobility Loss Energy Constructs).

The Pain-Energy Model consists of three separate premises, as illustrated in Figure 1.2.

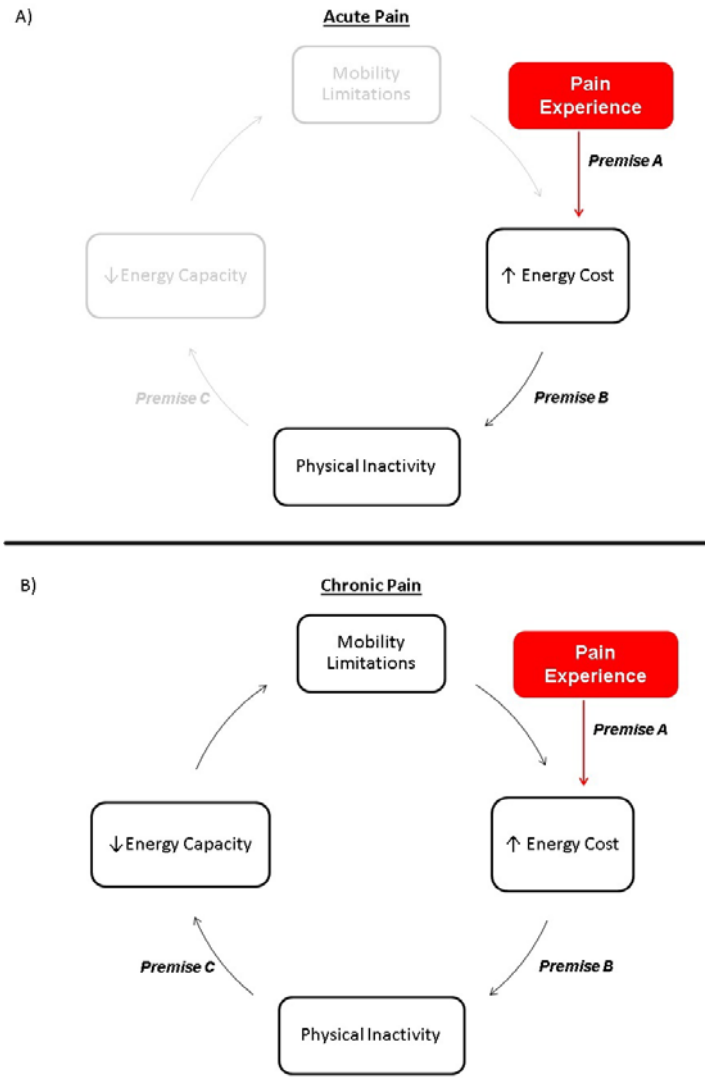

Figure 1.2: Illustration of the Pain-Energy Model with premises denoted. In Figure 1.2A, the impact that acute pain has on this pathway is displayed. Among older adults with painful conditions: A) the pain experience increases the energy cost of mobility (i.e. energetic inefficiency), B) increased energy cost of mobility contributes to physical inactivity. In Figure 1.2B, the long-term effects of pain are presented. With pain chronicity, C) persistent physical inactivity drives reductions in energy capacity. When energy capacity approaches the energetic cost of mobility, clinically relevant mobility limitations develop. These limitations, in turn, may contribute to increases in energy cost, further driving this disability cycle. Exacerbations of pain (i.e. acute-on-chronic) may also continue to drive this cycle.

We propose that, among older adults with acute pain, (Premise A) the pain experience increases the energy cost of functional mobility, and (Premise B) an increase in the energy cost of mobility leads to a restriction in physical activity. As pain persists, we hypothesize that (Premise C) long-term physical activity restrictions result in further reductions of energy capacity. We hypothesize that when pain is acute, the pain experience drives physical inactivity, in part, by energetic inefficiency without causing clinically relevant levels of functional mobility limitation; however, as pain and physical inactivity persist, energy capacity decreases to the point that it approaches energy cost of mobility, and functional mobility limitations develop. These limitations, in turn, may contribute to increased energy cost of mobility, further driving this disability cycle. Furthermore, exacerbations of chronically painful conditions (i.e. acute-on-chronic episodes) may also expedite this process.

Premise A: Pain experience increases energy cost of mobility. Previous work has shown that experimentally induced pain causes resting energy expenditure to rise by nearly 62%,[50] lending support to the hypothesis that acute painful sensations augment energy expenditure. Furthermore, these pain-related energetic alterations appear to carry over to fundamental activities, such as walking.[51-53] In one study, middle age and older adults with painful hip impairments were shown to expend more energy while walking than those without pain.[53] Similarly, Ko et al have shown that older adults with knee pain had a higher energy cost of walking than those without knee pain.[51] In patients with intermittent vascular claudication due to peripheral arterial disease, Gardner et al found that the energy cost of walking increased with acute pain onset and pain proliferation.[52] This evidence supports the hypothesis that

the pain experience may have a universal effect on energetic efficiency, particularly within older adults with chronically painful conditions.

Pain-related changes in motor strategies are likely the mechanism by which these changes in energy efficiency occur. Gait speed share a U-shaped relationship with walking economy.[30,54] Prior work has shown that one's natural self-selected gait speed is the most economical, requiring the least amount of energy per unit of distance.[30,54] Walking slower than one's self-selected pace may require less energy consumed per unit of time, but actually requires *more* energy over a given distance.[30,54] If experiencing pain causes a person to limit their speed for any reason, it may drive the person below their natural walking speed, increasing their energy consumed over a fixed distance. In support of this, Ko et al found that gait speed, along with knee range of motion, mediated the relationship between age and the energy cost of walking in older adults with knee pain.[51] Furthermore, pain may alter muscle activity during walking; for example, Ghamkhar & Kahlaee found that global trunk muscle activity increased during walking in those with chronic low back pain.[55] Increases in muscle activity likely comes at a higher energetic cost. In reality, each chronically painful condition may influence walking characteristics in a unique, condition-specific way; however, we contend that these gait impairments have a common influence on energy efficiency.

Premise B: Increases in the energy cost of functional mobility lead to a restriction in physical activity. There is a well-established body of literature that suggests that physical activity levels are attenuated in older adults with chronic pain.[56,57] Typically, this is thought to occur due in no small part to psychosocial factors (e.g. fear-avoidance).[58] While there is evidence to support this point, we

hypothesize that energetic inefficiency may also drive changes in physical activity levels.

Prior studies in mobility limited patient populations serve as the best evidence for the relationship between energy cost of mobility and physical activity behavior. Maltais et al found that, among people with cerebral palsy, worse walking economy strongly predicted lower physical activity levels.[59] In stroke survivors, prior work has shown that those with the highest levels of functional impairment have the greatest levels of energy cost of walking[60] and lowest physical activity levels,[61] compared to those with little functional mobility limitation. A recent study by Danks et al has shown that energy cost of walking is a strong predictor of daily step counts among stroke survivors.[62] Taken together, these studies suggest that energy efficiency and physical activity may be linked in other mobility-limited patient populations, such as those with painful conditions.

Premise C: Long-term physical activity restrictions result in further reductions of energy capacity. As previously noted, there is a body of literature to suggest that the overall physical activity levels of older adults with chronic pain are reduced.[56,57] Furthermore, the relationship between low physical activity and low energy capacity is well established.[63,64] Of course, it is important to note that the influence physical activity has on energy capacity is both quantity- and intensity-dependent. Yet, to our knowledge, there is no conclusive evidence that examines how specific painful conditions (e.g. knee osteoarthritis or chronic low back pain) influence the different components of physical activity, such as intensity. Although energy capacity has not been studied among older adults with chronic pain specifically, younger adults with chronic low back pain have been shown to have lower energy

capacity[65,66]; therefore, it is plausible that energy capacity is also reduced among geriatric chronic pain patients, given their low levels of physical activity.

The mechanisms by which physical inactivity leads to reductions in energy capacity are well documented, and involve both short-term and long-term physiological changes.[67,68] Abrupt decreases in physical activity causes central cardiovascular change (i.e. decreased heart function), while persistent physical inactivity causes changes in the peripheral cardiovascular system (i.e. impaired oxygen transport between vessels and muscles).[67,68] Further reductions in physical activity, such as those seen among older adults with painful conditions, may exacerbate these pathophysiological processes.

1.4 Significance and Implications of this Work

In Figure 1.3, we summarize the effects of the Pain-Energy model in the context of the Energetic Pathway to Mobility Loss.

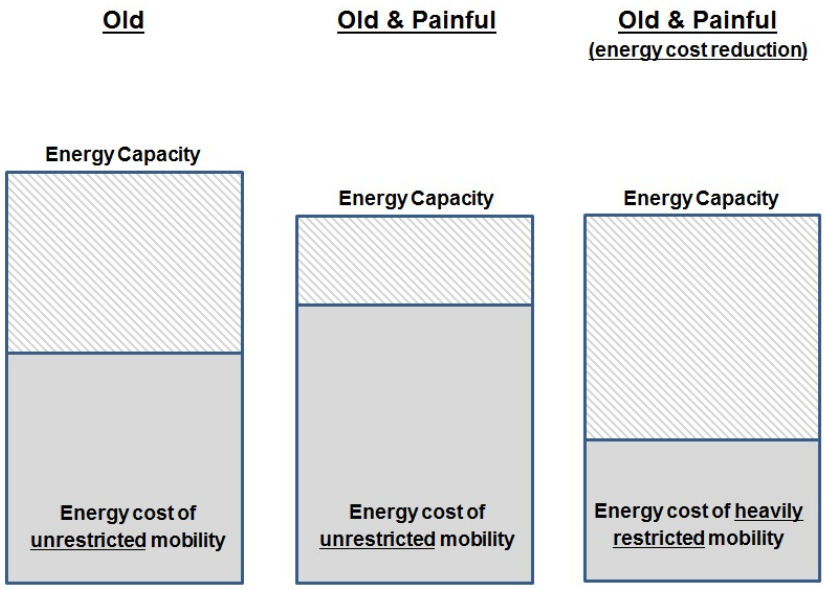

Figure 1.3: Illustration of the effects of the Pain-Energy Model in the context of Energetic Pathway to Mobility Loss. The pain experience increases the energy cost of unrestricted mobility while leading to decreases in energy capacity. As a compensatory strategy, mobility is heavily restricted to stay within the energy boundary.

The pain experience drives increases in the energy cost of mobility and decreases in energy capacity. As a result, functional mobility limitations develop to prevent energy cost from approaching energy capacity, thereby avoiding the risk of homeostatic collapse; however, the combined effects of both age and the pain experience result in even greater functional mobility limitations. Essentially, the pain experience accelerates the age-related decline of functional mobility.

It is important to note that limitations in functional mobility may arise from a number of different pathways, aside from energy expenditure.[69] For example, it has been clearly demonstrated that psychosocial factors play an important role in the pain

experience. A person with pain may be fearful of exacerbating their symptoms (i.e. fear-avoidance), choosing to reduce their overall physical activity, regardless of the impact that pain may have on the energy cost of mobility. While logical, we believe that the pathway from pain to mobility loss in the geriatric pain population is more complicated than driven purely by a psychosocial mechanism. While some individuals will immediately modify activities to limit pain, there are many who would choose to maintain an active lifestyle in spite of their pain, but are limited by an alternate pathway. The model that we propose is not meant to replace other models of disability development in this population, but rather propose a new pathway that has yet to be explored.

It is also important to note that, at present, this model is hypothetical, but very much logical given the current available evidence; it is meant to identify and generate a conceptual pathway by which pain may influence energy expenditure. It is wholly possible that the organization of the model may, in reality, be different from the causal order presented here. However, the current evidence supports the proposed pathway. Future systematic investigations need to be conducted to investigate the temporal and directional nature of these relationships to establish the validity of this model. Furthermore, future studies should investigate which aspects of the pain experience (e.g. pain frequency, intensity, interference) best predict adverse changes in energy expenditure. Regardless, this model still has important clinical implications.

Energy cost and capacity may be very important outcomes in the pathway to disability. As such, it may be beneficial to use these as outcomes to gauge treatment efficacy. Although measuring these outcomes requires specific tools (i.e. metabolic gas analysis equipment), these measurements are commonly performed in specific

clinical settings, such as cardiac rehabilitation centers. Collaboration between physical rehabilitation clinicians and exercise physiologists could allow for the implementation of these measurements among geriatric pain patients. Where such collaborations are not practical or possible, clinical tests exist to estimate energy capacity (i.e. VO2 Peak). For example, Simonsick et al found that the Long Distance Corridor Walk test, a test that requires minimal training, time, and equipment, can provide a valid estimate of Peak VO2 in older adults, by using a regression equation.[70]

This model also has important treatment implications. Pain management interventions should be utilized to decrease the instantaneous impact that pain provocation has on the energy cost of different activities. As mentioned, the energy cost of walking can be easily measured with metabolic gas analysis equipment; clinicians can measure walking economy to gauge treatment efficacy. Next, and perhaps more importantly, geriatric pain patients may benefit from interventions aimed at improving energetic efficiency (i.e. decrease energy cost) of mobility. This is important, because deficits in mobility often persist even after pain is effectively managed. For example, patients who have undergone total knee replacement surgery report great improvements in their pain, but have marginal improvements in mobility compared to pre-operative status,[71,72] and they continue to underperform compared to healthy older adults.[73] It is plausible that these patients continue to have higher levels of energy cost of mobility, despite resolution of their symptoms, due to compensation strategies that were learned as a result of their painful condition (e.g. impaired muscle coordination). Rehabilitation interventions exist for older adults that focus on the smoothness of walking to improve energetic efficiency,[74,75] but are not standard practice for those recovering from painful conditions. Considering the potentially

important role that increased energy cost of functional mobility plays in the disability pathway among older adults with pain, clinicians may consider incorporating intervention strategies that target impairments that may be contributing to increased energy cost.

Furthermore, clinicians may focus more heavily on physical activity interventions. Although this is not a new recommendation for the treatment of patients with chronic pain, past guidelines have simply advised clinicians to encourage their patients to be more physically active.[76] Physical activity interventions are effective at improving pain-related outcomes,[77-79] and clinicians may consider taking a more specific approach. Activity monitors are relatively inexpensive and easy to use. Clinicians may consider incorporating these instruments into their clinical practice to set goals and monitor patient progress. For example, prior research has shown that this is feasible to incorporate into clinical practice, and effective in improving daily walking activity in patients recovering from stroke.[80,81] Clinicians may also aim to improve or preserve energy capacity in older adults with chronic pain.[23,29] Energy capacity can be improved through a variety of different exercise interventions. For example, if a patient is unable to tolerate a specific mode of exercise, such as walking for knee osteoarthritis, then a clinician may use a mode of exercise that is less provocative, such as cycling, to improve energy capacity levels. Also, a mobility aid, such as a single point cane, may be used to prevent pain exacerbation and joint degradation, which can both lead to gait impairments; clinicians, however, should still emphasize that its' purpose is to allow the person to be more physically active, preserving energy capacity.

For clarity, we have included a glossary of key terms in Table 1.1.

Table 1.1: Glossary of key terms.

Term	Definition
Mobility limitation	Mobility limitations are "deficits in the ability to move or change body positions or location," which includes walking.[a]
Energy capacity	The upper limit of energy expenditure per minute available to perform vigorous activities. Often, this is measured by maximal or peak oxygen consumption during sustained, vigorous activity (VO_2 max or VO_2 peak, respectively).
Energy cost of mobility	The energy cost of walking and other mobility-related tasks (e.g. sit-to-stand transitions, stair climbing, etc). Energy expenditure is commonly measured by analyzing the amount of oxygen one consumes during aerobic activity.
VO_2	The volume of oxygen consumed during submaximal or maximal (i.e. *VO_2 max* or peak) aerobic activity. Also known as indirect calorimetry, and it is quantified as the amount of oxygen consumed in milliliters per kilogram of bodyweight per minute (ml/kg/min).
Pain experience	"An unpleasant sensory and emotional experience associated with actual or potential damage, or described in terms of such damage."[b]
Daily physical activity	Any bodily movement produced by skeletal muscles that requires energy expenditure.[c]

[a] From the World Health Organization, 2001.
[b] From the International Association for the Study of Pain, 2016.
[c] From the World Health Organization, 2016.

1.5 Specific Aims

The overall goal of this work is to test specific relationships and hypotheses contained within this conceptual model in different patient populations. We are proposing to investigate Specific Aims 1-3 by conducting a comparative, cross-sectional case-control study of two groups of older adults: 21 with and 21 without

chronic low back pain with radiculopathy (CLBPR), or pain that radiates to or below the knee. Not only is this condition prevalent among older adults, but symptoms can be reliably provoked with walking, which poses significant mobility challenges. Specific Aim 4 will be explored by conducting a secondary analysis of a rich, longitudinal dataset, which contains information on the lumbopelvic pain status of older adults, as well as specific energy expenditure measures. The specific aims of this project are to determine whether:

AIM 1: Older adults with CLBPR have greater impairments in energy expenditure, and whether these impairments will worsen with pain provocation compared to pain-free older adults.

- Hypothesis 1.1: Older adults with CLBPR will have a greater energy cost of walking (i.e. energy inefficiency) during walking at self-selected speed, compared to pain-free, matched controls.
- Hypothesis 1.2 Older adults CLBPR will achieve lower Peak Walking VO2 values during a fast-pace walking test of energy capacity, compared to pain-free, matched controls.
- Hypothesis 1.3 Higher energy cost of walking will be cross-sectionally related to Peak Walking VO2 after controlling for suspected covariates, but this relationship will be stronger among those with CLBPR.
- Hypothesis 1.4: Older adults with CLBPR, who exhibit a clinically meaningful increase in pain while walking, will have a greater energy cost of walking in late compared to early stages of walking, but this factor will remain unchanged in those who do not exhibit this change in pain intensity or are pain-free.
- Hypothesis 1.5 Among older CLBPR, who exhibit a clinically meaningful increase in pain, increases in pain intensity from early to late stages of walking, will be related to increases in the energy cost of walking.

AIM 2: Older adults with CLBPR will demonstrate lower levels of physical activity and increased inactivity compared to pain-free older adults in a descriptive analysis of step activity monitoring.

- Hypothesis 2.1: Older adults with CLBPR who experience a clinically relevant increase in their pain with walking, will have a significantly different quintile distribution from those who do not experience a significant increase in their pain and pain-free peers, in the following daily physical activity structural characteristics:
    - Hypothesis 2.1a: steps per walking bout (raw bout count)
    - Hypothesis 2.1b: steps per walking bout (percent of total bouts)
    - Hypothesis 2.1c: average cadence per walking bout (raw bout count)
    - Hypothesis 2.1c: average cadence per walking bout (percent of total bouts)
- Hypothesis 2.2: Older adults with CLBPR who experience a clinically relevant increase in their pain with walking, will have reduced levels of activity compared to those who do not experience a significant increase in pain and matched, pain-free peers, in the following physical activity summary characteristics:
    - Hypothesis 2.2a: median walking bout duration
    - Hypothesis 2.2b: median steps per walking bout
    - Hypothesis 2.2c: median cadence per walking bout
    - Hypothesis 2.2d: median inactive bout duration
    - Hypothesis 2.2e: total walking bouts per day
    - Hypothesis 2.2f: total inactive bouts per day
    - Hypothesis 2.2g: average steps per day

- Hypothesis 2.2h: average time spent walking per day
- Hypothesis 2.2i: average time spent inactive per day
- Hypothesis 2.2j: average percent of wear time spent walking per day

AIM 3: Deficits in energy efficiency are associated with decreased physical activity levels and increased inactivity in older adults with CLBPR, and these relationships will be moderated by the provocation status of their symptoms.

- Hypothesis 3.1: Among older adults with CLBPR, increases in the energy cost of walking at self-selected speed will be associated with the following:
  - Hypothesis 3.1a: lower median walking bout duration.
  - Hypothesis 3.1b: lower median steps per walking bout.
  - Hypothesis 3.1c: lower median cadence per walking bout.
  - Hypothesis 3.1d: higher median inactive bout duration.
  - Hypothesis 3.1e: less total walking bouts per day.
  - Hypothesis 3.1f: more total inactive bouts per day.
  - Hypothesis 3.1g: less average total steps per day.
  - Hypothesis 3.1h: less average time spent walking per day.
  - Hypothesis 3.1i: more average time spent inactive per day.
  - Hypothesis 3.1j: lower average percent of wear time spent walking per day.
- Hypothesis 3.2: The relationships listed above are moderated by pain provocation status (i.e. experiences a clinically relevant increase in pain intensity during walking) of older adults with CLBPR.

AIM 4: Deficits in energetic efficiency are predictive of declines in energetic capacity over time, and if lumbopelvic pain intensity status will moderate this relationship, in a population-based study, the Baltimore Longitudinal Study of Aging.

- Hypothesis 4.1: Among older adults, higher baseline energy cost of walking will be predictive of declines in Peak Walking VO2 over time, regardless of the presence of lumbopelvic pain.

- Hypothesis 4.2: Pain intensity will moderate the relationship between higher baseline energy cost of walking and decline in Peak Walking VO2 among older adults with lumbopelvic pain, such that those with severe lumbopelvic pain will exhibit greater reductions in energy capacity for each unit increase in the baseline energy cost of walking.

Chapter 2

THE CHRONIC EFFECTS OF LOW BACK AND RADICULAR LEG PAIN ON ENERGY EFFICIENCY AND ENERGY CAPACITY

2.1 Introduction

Chronically painful conditions are common,[82] costly,[2,4] and detrimental to the quality of life of older adults.[6,8,10,83,84] Chronic low back pain with radiculopathy (CLBPR), which is pain that radiates from the lumbar spine into the leg(s), is particularly common among older adults,[6,85] because this clinical presentation is often consistent with age-enhanced, degenerative changes of the spine. A hallmark sign of this condition is pain that worsens with upright posture, leading to significant walking impairments.[6,85] Aspects of walking, such as walking speed, are strongly predictive of disability[12,13] and mortality in the elderly,[14,15] which make this an important clinical population to target for intervention.

Walking speed naturally declines with age,[86,87] although the reasons why this happens are not exactly clear. Recently, gerontological researchers have shown that age-related declines in walking speed may be driven, in part, by changes in energetic efficiency and capacity, which can be measured by indirect calorimetry (i.e. oxygen consumption).[27-29,46] Energy capacity is the upper limit of energy able to be expended per minute during vigorous activity, and it is typically measured as peak oxygen uptake (Peak Walking VO2) during walking at one's fastest speed; energy efficiency is the energetic cost of movement, and it is measured as the amount of oxygen consumed per meter walked, at self-selected speed.[27-29,46] Energy capacity[31] and the

energetic efficiency of movement[34,88] deteriorate with age. In our conceptual model, the Pain-Energy model of mobility limitation (see Chapter 1),[89] we hypothesize that pain drives energy inefficiency and diminishes energy capacity, in turn, contributing to the development of mobility limitations.

Recent work has shown that these two energetic constructs work in tandem with one another, and that they may drive the age-related decline of functional mobility.[29] Schrack et al proposed that inefficiencies associated with age may contribute to reduced activity, and slowed movement to conserve energy; this behavior may contribute to the age-related decline of energy capacity, causing a person to use a higher proportion of their capacity for activities of daily living.[27,29] Indeed, energy efficiency is related to slow walking in those with low energetic capacity.[29] Yet this hypothesis suggests that there is a relationship between energy efficiency and capacity, but this has not been explored.

Chronically painful conditions of the low back and legs have been shown to be linked to slower walking speeds among older adults,[7,10,17-20] thereby increasing the risk of adverse health outcomes. Pain may have a unique impact on energy efficiency and capacity, which may, in turn, contribute to the mobility limitations associated with painful conditions. Prior work has shown that walking comes at an elevated energetic cost among those with painful conditions of the hip[53] and knee.[51] Additionally, there is evidence to suggest that those with localized chronic low back pain have a lower energy capacity, but this work was completed in middle-aged rather than older adults.[65,66] There is some literature that suggests that those with CLBPR are less active,[90-93] and physical inactivity is strongly linked to poor energy capacity.[63,64] Thus, it is plausible that CLBPR results in impaired energetic capacity, through a pathway of

physical inactivity. However, there are no studies, to our knowledge, that have examined how this condition directly influences energy efficiency and capacity.

The first purpose of this study was to investigate how CLBPR influences the energetic efficiency of walking and energy capacity. The second purpose was to examine the potential relationship between energy efficiency and capacity among those with and without CLBPR. We hypothesized that older adults with CLBPR would have a higher energy cost of walking at self-selected speed (i.e. worse energy efficiency), as well as reduced Peak Walking VO2 (i.e. worse energy capacity), compared to age- and sex-matched, pain-free participants. Furthermore, we hypothesized that higher energy cost of walking would be linked to reductions in Peak Walking VO2 after controlling for potential covariates, and that this relationship would be stronger in those with CLBPR.

2.2 Methods

2.2.1 Participants

This study was a comparative analysis of a sample of community-dwelling, cognitively intact (Folstein Mini-Mental State Exam score ≥ 18)[94] older adults with and without CLBPR. For the purposes of this study, this age group was defined as 60-85 years old. Participants with CLBPR recruited for this study met the following pain criteria: low back pain intensity ≥3/10, pain frequency ≥4 days per week, pain duration ≥3 months, and pain that radiated into the legs (at, or below, the knee) with walking. Participants with pain were excluded if they had any of the following: non-mechanical low back pain symptoms (e.g. unrelenting night pain, lack of sensation in the groin and/or buttocks), severely limited mobility (i.e. needed an assistive device for testing),

significant cardiovascular or cardiopulmonary disease, a progressive neurological disorder, or a terminal illness.

Pain-free older adults were included if they did not have low back pain within the year prior to participation, or any significant areas of pain in the 72 hours preceding the study evaluation. Furthermore, they must have matched a CLBPR participant already enrolled in the study based on the following characteristics: age (± 5 years), sex, and diabetes status. These individuals were excluded for the same criteria as mentioned for older adults with CLBPR.

All participants were recruited from newspaper advertisements, local senior centers, health fairs, and local physician and physical therapy clinics. Seventy-eight people were screened, 36 were either excluded or not interested in participating, and 42 participants were enrolled in the study. Two participants from the CLBPR group did not have complete data for these analyses; one participant refused part of the testing, and another did not complete enough of the testing protocol to provide valid data. These two participants and their pain-free, matched peers were removed from the analysis, leaving a total sample size of 38 participants. All policies and procedures were followed in accordance with the proposal approved by the University of Delaware Institutional Review Board and the Helsinki Declaration of the World Medical Association. All participants signed an informed consent form, and consent forms were securely stored.

2.2.2 Demographics and Self-Ratings

Participants reported their age, sex, and diabetes status. Height and weight were measured with the participant's shoes off using a Healthometer Professional™ digital scale (Mohawk Medical, Utica, NY), and body mass index was calculated. The

modified Quebec Disability Index (QDI) was used to measure low back pain-related disability.[95] The numeric pain rating scale[96] was used to measure worst pain intensity in the last 24 hours in both low back and leg(s), with anchors from 0 ("no pain") to 10 ("worst possible pain"). The Borg Rating of Perceived Exertion (RPE) scale was used to measure self-reported exertion (scores range 6-20), with lower scores indicating lower levels of exertion.[97] RPE was measured throughout the protocol as described in the following sections.

2.2.3 Energy Cost of Walking at Self-Selected Speed

The energy cost of walking, which is the amount of energy consumed per unit of distance, was measured using metabolic gas analysis equipment. The energy cost of walking was derived by using the following formula:

$$Energy\ Cost\ of\ Walking = \frac{Average\ VO2}{Walking\ Speed} = \frac{mL\ O2/kg\ body\ weight/min}{meters/min}$$

The energy cost of walking at self-selected speed has been used to measure energetic efficiency in other studies.[27,28,46] Prior work has shown that the most energetically efficient walking speed for healthy, older adults occurs close to their normal self-selected pace. Schrack et al found normal energy cost values were approximately .170 and .195 mL/kg/meter for older adults aged 60 and 80 years, respectively.[28]

In this study, the energy cost of walking was assessed by measuring oxygen (VO2) consumption (mL/kg/min) during a walking test, conducted at the participant's self-selected speed around a marked course with a known distance. The test was conducted in a closed corridor, as participants walked back and forth around two traffic cones that were separated by 20 meters. Participants were required to walk 2.5 minutes while VO2 consumption was measured. This method is similar to energy cost

of walking measurements taken in other studies of community-dwelling, older adults.[27-29,46]

The Oxycon Mobile™ Portable VO2 Measurement system (CareFusion™, San Diego, CA) was used to measure VO2 consumption. In brief, the Oxycon Mobilie™ unit uses a rubber facemask and turbine for gas collection, allowing for over ground ambulation. Per CareFusion™ recommendations, this device was calibrated at the beginning of each test using standard calibration gases (16% O2, 4% CO2, balance nitrogen) for gas content, and the auto-calibration function for gas flow.

VO2 consumption was recorded using the single breath format, and then averaged for each 20 meter interval. Data from the first 1.5 minutes of collection were discarded to ensure the participant reached physiologic steady state; data from the remaining 1-minute window (i.e. 1.5-2.5 minute mark) were used for these analyses. VO2 consumption from each breath in the 1-minute window was averaged. The duration of each length was recorded; gait speed was calculated for each length by dividing 20 meters by the length duration. Gait speed values, from the lengths included in this 1-minute window, were averaged to arrive at a single value. The energy cost of walking (mL/kg/m) was calculated by dividing VO2 consumption by average gait speed (meters/minute), as indicated in the formula above.

2.2.3.1 Secondary Outcomes

Average VO2 consumption and average gait speed were considered secondary outcomes. In addition, the metabolic gas analysis device also computed Respiratory Exchange Ratio (RER) for each breath taken; RER is the ratio of CO2 produced to VO2, and it is indicative of metabolic exertion.[98] RER values included in the 1-minute

window were averaged. RPE was recorded for each length, and the RPE values for the lengths included in this 1-minute window were averaged for a single measurement.

2.2.4 Peak Walking VO2

Peak Walking VO2 was captured during a 400-meter walk test at peak sustained walking speed. Prior research has shown that values that fall below a threshold of approximately 18 mL/kg/min suggest a greater risk of disability.[23] Using the same course as previously described, this 400-meter walk test was conducted. This test has been validated as a measure of cardiorespiratory fitness in older adults,[70] and this protocol was identical to that of a previous study on aging and energy expenditure.[27,29] After a seated rest period of at least 5 minutes, participants were instructed to walk as *fast* as they could around the cones for 10 full laps, for a total of 400 meters. Standardized encouragement was given at each lap.

VO2 consumption was measured using the same equipment and parameters as previously described. Again, data from the first 1.5 minutes were discarded to ensure the participant reached physiologic steady state. To calculate Peak Walking VO2, the remaining VO2 consumption values measured from each breath taken during the duration of the test, were averaged. This method for measuring energy capacity is consistent with previous literature on geriatric energy expenditure.[27,29] If participants were unable to complete the fast speed walking test, the usable data before the walk test ended was averaged for a Peak Walking VO2 measurement; this required a minimum of 30 seconds of usable VO2 measurements. Gait speed was computed as the distance covered during the test divided by the time (in seconds) it took to complete the test.

2.2.4.1 Secondary Outcomes

Average energy cost of fast speed walking was calculated from Peak Walking VO2 and average gait speed. In addition, RER was measured for each breath in the same time window as Peak Walking VO2, and these values were averaged to arrive at a single measure. RPE was measured immediately after the conclusion of this test.

2.2.5 Statistical Analysis

Statistical analyses were performed using SPSS 24 (SPSS, Inc. Armonk, NY). Descriptive analyses were performed for both groups, including demographic characteristics, diabetes status, and pain-related disability. Two different inferential statistical tests were used. First, a mixed-design analysis of covariance (ANCOVA) that controlled that controlled for body mass index was used, because the groups had a clinically relevant difference in average body mass index. Pairwise, between-group comparisons were made for both the energy cost of walking at self-selected speed and Peak Walking VO2. Second, linear regression was used to examine the potential relationship between the energy cost of walking at self-selected speed and Peak Walking VO2, as well as the potential moderation effect that CLBPR status had on this relationship after adjusting for covariates. Peak Walking VO2 was designated as the dependent variable. Participant age, sex, body mass index, and diabetes status were entered into the first step as suspected covariates. Then, the main effect for group status was entered. Next, the main effect for the energy cost of walking during self-selected speed was entered. Finally, an interaction term for group status and the energy cost of walking at self-selected speed was entered into the final step of the model. For all analyses, α=.050.

2.3 Results

Table 2.1 displays the descriptive characteristics for both groups. As previously mentioned, participants were matched on age (± 5 years), sex, and diabetes status. The difference in body mass index was not statistically significant (p=.087), but it was clinically relevant; those with CLBPR were considered 'obese' on average, while those who were pain-free were considered 'overweight'. Given these findings, the conservative approach to include it as a covariate was then employed. Participants experienced an average score of 34.4 on the Quebec Disability Index, indicating moderate low back pain-related disability.

Table 2.1: Descriptive characteristics

	Control (n=19)	**CLBPR (n=19)**
	n (%)	
Female	10 (52.6)	10 (52.6)
Diabetic	4 (21.1)	4 (21.1)
	Mean (SD)	
Age	68.9 (5.8)	68.8 (4.8)
BMI	27.9 (4.1)	30.8 (8.3)
Duration of LBP (years)	-	12.8 (15.0)
Duration of Leg Pain (years)	-	3.8 (5.2)
Worst LBP Intensity (0-10)	-	6.2 (2.5)
Worst Leg Pain Intensity (0-10)	-	6.0 (3.0)
Quebec (0-100%)	-	34.4 (17.5)

*p≤.050

Abbreviations: CLBPR = Chronic low back pain with radiculopathy; BMI = body mass index; LBP = low back pain; Quebec = Quebec Disability Index

Figure 2.1 illustrates the results from the pairwise, between-group comparisons for the energy cost of walking at self-selected speed and Peak Walking VO2. In

addition, these results, along with the between-group comparisons of the secondary outcomes for each test, are presented in separate tables.

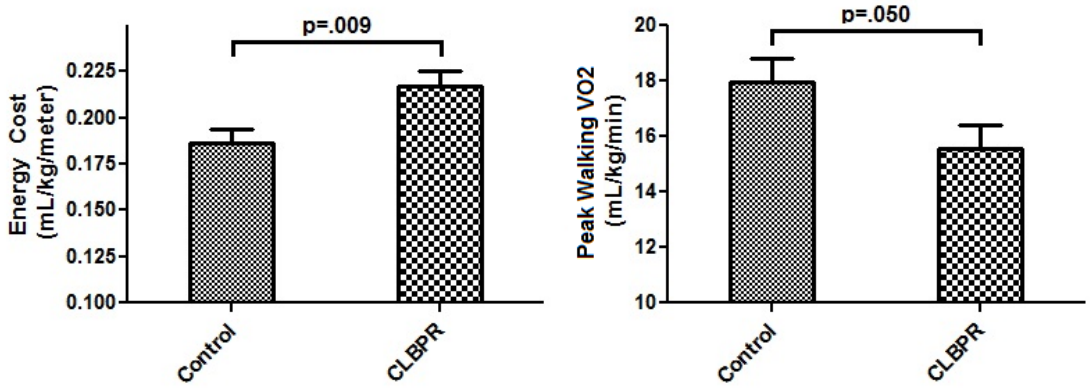

Figure 2.1: Between-group differences in energy cost of walking and Peak Walking VO2, adjusted for body mass index

Table 2.2 displays the results from the between-groups comparison for the energy cost of walking at self-selected speed and the secondary outcomes associated with that measurement. Control participants had a lower energy cost of walking at self-selected speed compared to those with CLBPR (absolute mean difference = .031 mL/kg/meter, p=.009). Pain-free controls walked significantly faster than those with CLBPR (absolute mean difference = .14 m/sec, p=.003); VO2 consumption was similar between groups. RER and RPE did not differ significantly between groups. To satisfy the assumption of normality of residuals, two outliers from the pain group, as well as their matched controls, were removed for the VO2 consumption comparison.

Table 2.2: Between-group differences for the energy cost of walking at self-selected speed and associated secondary outcomes, adjusted for body mass index

	Control (n=19)	CLBPR (n=19)		
	Adjusted Mean (SE)		Partial Eta Squared	p-value
Energy Cost of Walking at Self-Selected Speed (mL/kg/m)	0.186 (.008)	.217 (.008)	.181	.009*
VO2 (mL/kg/min)†	12.51 (5.25)	12.44 (5.25)	.000	.992
Gait Speed (m/sec)	1.11 (.031)	.97 (.031)	.195	.003*
Respiratory Exchange Ratio	0.784 (.010)	.807 (.010)	.067	.121
Rating of Perceived Exertion‡	7.4 (.3)	8.3 (.3)	.099	.065

*p≤.050
†1 outlier was removed from each group
‡1 participant in CLBPR did not rate RPE, and matched-control was removed (n=18 for both groups)
Abbreviations: CLBPR = Chronic low back pain with radiculopathy

Table 2.3 displays the results from the between-groups comparison for Peak Walking VO2 and the secondary outcomes associated with that measurement. Those with CLBPR had a significantly lower Peak Walking VO2 than controls, (absolute mean difference = .2.39 mL/kg/min, p=.050). In addition, the energy cost of walking at fast speed did not differ between groups; however, those with CLBPR walked significantly slower than matched, pain-free controls (absolute mean difference = .28 m/sec, p=.002). The two groups did not differ significantly in RER or RPE. To satisfy the assumption of normality of residuals for Peak Walking VO2 comparison, one outlier was removed from both groups.

Table 2.3: Between-group differences for Peak Walking VO2 and associated secondary outcomes, adjusted for body mass index

	Control (n=19)	CLBRP (n=19)		
	Adjusted Mean (SE)		Partial Eta Squared	p-value
Peak Walking VO2 (mL/kg/min)†	17.97 (.82)	15.58 (.82)	.111	.050*
Energy Cost of Walking at Fast Speed (mL/kg/m)	.198 (.007)	.212 (.007)	.053	.171
Gait Speed (m/sec)	1.55 (.06)	1.27 (.06)	.253	.002*
Respiratory Exchange Ratio	.951 (.027)	.924 (.027)	.013	.499
Rating of Perceived Exertion‡	13.1 (.6)	14.5 (.6)	.079	.092

*p≤.050
†1 outlier was removed from each group
‡1 participant in CLBPR did not rate RPE, and matched control was removed (n=18 for both groups)
Abbreviations: CLBPR = Chronic low back pain with radiculopathy

Table 2.4 displays the results from the linear regression analysis, which examined the relationship between Peak Walking VO2 and the energy cost of walking at self-selected speed; the potential interaction between group assignment and the energy cost of walking at self-selected speed was also explored. Potential covariates accounted for 26.7% of the variance in the energy cost of walking (p=.032). However, neither the main effect for group, the main effect for the energy cost of walking at self-selected speed, nor the interaction between the two, made a significant contribution to the variance explained in Peak Walking VO2.

Table 2.4: Relationship between Peak Walking VO2 and energy cost of walking at self-selected speed, adjusted for suspected covariates (n=38)

Model	Independent Variables	R^2 Change	Adjusted R^2	p-change
1	Age, Sex, BMI, Diabetes Presence	.267	.178	.032*
2	Model 1 + Group	.082	.247	.053
3	Model 2 + Energy Cost of Walking at Self-Selected Speed	.055	.289	.100
4	Model 3 + Energy Cost of Walking at Self-Selected Speed x Group Interaction	.007	.274	.553
Unstandardized β (p-value) for Interaction Term: -28.974 (.553)				

*p≤.050
Abbreviations: BMI = Body mass index

2.4 Discussion

The purpose of this study was to determine the potential impact that CLBPR had on energy efficiency and capacity among older adults. In addition, we examined the potential, cross-sectional relationship between energy efficiency and capacity, while controlling for covariates, in older adults with and without CLBPR. Our results suggest that CLBPR negatively impacts both the energy cost of walking at self-selected speed and Peak Walking VO2 among older adults, suggesting that CLBPR is associated with energy inefficiency and diminished energy capacity. In this study, a relationship between energy efficiency and capacity was not seen, and there was no indication that the presence of CLBPR moderated that potential relationship.

To our knowledge, this is the first study to establish a link between energy inefficiency and CLBPR among older adults. CLBPR contributes to gait impairments that may be unique to this condition.[99,100] Optimal mechanics contribute to energy efficiency[101], while gait alterations can reduce efficiency.[88] Because walking typically

provokes symptoms in those with CLBPR, it is plausible that pain provocation alone may contribute to the worsening of gait mechanics. Gardner et al found that among those with peripheral arterial disease, pain onset during walking due to intermittent vascular claudication in individuals with peripheral arterial disease, contributed to gait asymmetry in different phases of walking[102]; however, Myers et al found no difference in the kinematics of walking in painful compared to pain-free states in individuals with peripheral arterial disease.[103] Regardless, the energy cost measurements in our study were taken within the first 2.5 minutes of walking when symptoms were at the minimum; therefore, these energetic inefficiencies observed were not likely due to the provocation of symptoms alone. In fact, in the Pain-Energy conceptual model, we hypothesized that acute and chronic pain have unique effects on the Energetic Pathway to Mobility Loss.[89] These findings lend support to the chronic pain portion of this model; future studies should investigate the acute pain component of this model.

This study is also the first to identify the impact that CLBPR has on energy capacity, as Peak Walking VO2 was found to be lower in this group. Prior work has suggested that a Peak Walking VO2 lower than 18 mL/kg/min is predictive of developing difficulty in some aspects of physical function[24]; our results show that those with CLBPR fall firmly below this threshold, suggesting that these individuals are at a higher risk for the development of disability. However, it is reasonable for one to suspect that those with CLBPR did not achieve as high a level of metabolic exertion simply because walking is provocative to their symptoms, and not because they possess a lower energetic capacity. If this were true, we would expect those without pain to achieve a significantly higher level of metabolic exertion than those with CLBPR, indicating that pain prevented those with CLBPR from “pushing

themselves". However, the RER measurements, which are an indication of the level of metabolic exertion,[98] were found to be similar between the two groups; this indicates that the energy capacity of older adults with CLBPR was, in fact, lower than their pain-free peers.

Schrack et al hypothesized that energy efficiency may drive reductions in energy capacity among older adults, via physical inactivity.[27,29] Therefore, we hypothesized that energy inefficiency would be linked to lower energy capacity. Although our results suggest that energy efficiency and capacity are reduced in those with CLBPR, they do not suggest that there is a relationship between the two constructs. This finding, or lack thereof, is perplexing. Of course, there may, in fact, be no relationship between these two variables. However, if there is a relationship, we may have failed to detect it for two reasons. First, the effect size of the relationship may be smaller than projected, and we were underpowered to detect it. Post-hoc power analyses indicate that a sample size of 137 would be needed to detect a relationship between the energy cost of walking at self-selected speed and Peak Walking VO2 with an R^2 Change = .055, α = .050, and power = 80%. Second, we made the assumption that walking at self-selected speed is the most efficient for both groups, due to a body of literature that suggests this is the most economical pace for a person.[30,34,54] Upon further investigation of our data, we found that while our control group demonstrated that expected pattern, those with CLBPR actually became *more* efficient in the fast speed walking test, compared to the self-selected test. These results can be seen when comparing Tables 2.2 and 2.3. This result is unexpected and warrants further investigation.

This work has important clinical implications. First, energy inefficiency may be a potentially important factor to target in rehabilitation. Prior work has shown that there are effective rehabilitation strategies, such as interventions that focus on the timing and coordination of walking, to improve the energy efficiency of walking among older adults[74,75]; patients with CLBPR may be an important clinical population on which to use these treatment strategies. The fact that fast-pace walking appears to be more efficient in those with CLBPR suggests that encouraging them to walk faster may be an effective strategy for improving the energy cost of walking. Second, energy capacity may also be a potentially important factor to focus on in the rehabilitation of older adults with CLBPR. Not only is low Peak Walking VO2 predictive of mortality,[25,104] but it also plays a specific role in the context of reduced walking speed[29] and functional limitations[23,24]; improving Peak Walking VO2 may combat the onset and/or the progression of disability.

In addition to having a limited sample size, this study has limitations. This sample of older adults with CLBPR was high-functioning with regard to their mobility. The testing protocol required individuals to be able to walk for long periods of time without the use of an assistive walking device. Also, in order to isolate the impact that this condition had on these measures, we had to exclude individuals with significant comorbidities, as they may have confounded the results. Future studies should repeat these analyses in a larger, more representative sample of older adults with CLBPR. Finally, in this discussion section we speculate that the energy inefficiency observed in the pain group may have arose from gait impairments. However, kinematic motion analysis was not feasible, given the space requirements needed to perform the walking tests.

2.5 Conclusion

Older adults with CLBPR are energetically inefficient and have a diminished energy capacity, compared to older adults without pain. Among those with CLBPR, fast-paced walking appears to be more efficient, which warrants further investigation. Regardless, these two energetic factors are potentially modifiable, and are linked to mobility limitation; clinicians may focus on them to reduce the risk of onset and/or progression of disability.

Chapter 3

CHANGES IN ENERGY EFFICIENCY AMONG OLDER ADULTS WITH AND WITHOUT CHRONIC LOW BACK AND RADICULAR LEG PAIN: A COMPARISON STUDY

3.1 Introduction

Chronically painful conditions are common,[82] costly,[2,4] and detrimental to the quality of life of older adults.[6,8,10,83,84] Chronic low back pain with radiculopathy (CLBPR), which is pain that radiates from the lumbar spine into the leg(s), is particularly common among older adults,[6,85] because this clinical presentation is often consistent with age-enhanced, degenerative changes of the spine. A hallmark sign of this condition is pain that worsens with upright posture and ambulation, leading to significant walking impairments.[6,85] Aspects of walking, such as walking speed, are strongly predictive of disability[12,13] and mortality in the elderly.[14,15] Consequently, older adults with CLBPR are an elevated risk for adverse health events due to these functional deficits.

Energetic impairments are emerging in the gerontological research literature as potentially important factors in the age-related decline of walking speed.[27-29,46] In a robust, longitudinal study of community-dwelling older adults, Schrack et al showed that poor energy efficiency of walking was predictive of declines in walking speed, and that energy inefficiency was associated with a 57% greater risk of developing slow walking speed, compared to a normal energy efficiency.[46] Chronically painful

conditions of the low back and legs tend to amplify these reductions in walking speed,[7,10,17-20] thereby increasing the risk of adverse health outcomes.

Prior conceptual models of disability development in chronic pain populations suggest that psychosocial factors (e.g. fear-avoidance) drive mobility limitations through a pathway of physical inactivity,[21] but the physiological underpinnings of pain are largely unexplored. In our conceptual framework, the Pain-Energy Model, we have proposed that the pain experience has unique impact on energetic factors, driving the development of mobility limitations.[89] Our prior work has shown that the presence of CLBPR is linked to worse energy efficiency among older adults (see Chapter 2), but the impact that acute pain provocation has on energy efficiency remains unknown. Holland-Fischer et al found that experimentally induced pain caused resting energy expenditure to rise.[50] Gardener et al has shown that the mere onset of pain due to intermittent vascular claudication related to peripheral arterial disease, led to worse energy efficiency of walking.[52] If pain provocation does have a significant impact on energy efficiency in older adults with CLBPR, then this may be an important characteristic to target for intervention in attenuating mobility deterioration; these findings would be consistent with the pathway proposed in the Pain-Energy model.

The primary purpose of our study was to examine the impact that pain provocation had on the energy cost of walking at self-speed (i.e. energy efficiency) in older adults with CLBPR, compared to that of pain-free individuals. We hypothesized that clinically relevant increases in pain intensity would drive increases in the energy cost of walking in older adults with CLBPR. We also hypothesized that energy cost would not change over a similar period of time in age- and sex-matched, pain-free peers, as well as individuals with CLBPR who did not experience a clinically

meaningful increase in pain. Finally, we hypothesized that greater increases in pain intensity would be linked to greater increases in the energy cost of walking, even after controlling for known covariates, among those with CLBPR who experience a clinically relevant increase in pain.

3.2 Methods

3.2.1 Participants

This study was a comparative analysis of a sample of community-dwelling, cognitively intact (Folstein Mini-Mental State Exam score ≥ 18)[94] older adults with and without CLBPR. For the purposes of this study, this age group was defined as 60-85 years old. Participants with CLBPR recruited for this study met the following pain criteria: low back pain intensity ≥3/10, pain frequency ≥4 days per week, pain duration ≥3 months, and pain that radiated into the legs (at, or below, the knee) with walking. Participants with pain were excluded if they had any of the following: non-mechanical low back pain symptoms (e.g. unrelenting night pain, lack of sensation in the groin and/or buttocks, etc), severely limited mobility (i.e. needed an assistive device for testing), significant cardiovascular or cardiopulmonary disease, a progressive neurological disorder, or a terminal illness.

Pain-free older adults were included if they did not have low back pain within the year prior to participation, or any significant areas of pain in the 72 hours preceding the study evaluation. Furthermore, they must have matched a CLBPR participant already enrolled in the study based on the following characteristics: age (± 5 years), sex, and diabetes status. These individuals were excluded for the same criteria as mentioned for older adults with CLBPR.

All participants were recruited from newspaper advertisements, local senior centers, health fairs, and local physician and physical therapy clinics. Seventy-eight people were screened, 36 were either excluded or not interested in participating, and 42 were enrolled in the study. Participants from the CLBPR and pain-free groups were matched based on age (± 5 years), sex, and diabetes status. All policies and procedures were followed in accordance with the proposal approved by the University of Delaware Institutional Review Board and the Helsinki Declaration of the World Medical Association. All participants signed an informed consent form, and consent forms were securely stored.

3.2.2 Demographics and Self-Ratings

Participants reported their age, sex, diabetes status, and duration of both low back and leg pain. Height and weight were measured with the participant's shoes off using a Healthometer Professional™ digital scale (Mohawk Medical, Utica, NY), and body mass index was calculated. The modified Quebec Disability Index (QDI) was used to measure low back pain-related disability.[95] The numeric pain rating scale was used to measure pain intensity with anchors from 0 ("no pain") to 10 ("worst possible pain").[96] The Borg Rating of Perceived Exertion (RPE) scale was used to measure self-reported exertion (scores range 6-20), with lower scores indicating lower levels of perceived exertion.[97] Pain intensity ratings and RPE were measured throughout the energy cost of walking test protocol as specified in the following section.

3.2.3 Energy Cost of Walking

The energy cost of walking, which is the amount of energy consumed per unit of distance, was measured using metabolic gas analysis equipment. The energy cost of walking (mL/kg/min) was derived by using the following formula:

$$Energy\ Cost\ of\ Walking = \frac{Average\ VO2}{Walking\ Speed} = \frac{mL\ O2/kg\ body\ weight/min}{meters/min}$$

The energy cost of walking at self-selected speed has been used to measure energetic efficiency in other studies.[27,28,46] Prior work has shown that the most energetically efficient walking speed for healthy, older adults occurs close to their normal self-selected pace.[54]

In this study, the energy cost of walking was assessed by measuring oxygen (VO2) consumption (mL/kg/min) during a walking test, conducted at the participant's self-selected speed, around a marked course with a known distance. The testing protocol was adapted from a similar study in peripheral arterial disease patients by Gardner et al.[52] The test was conducted in a closed corridor, as participants walked back and forth around two traffic cones that were separated by 20 meters. Participants were instructed to walk at their usual, comfortable pace until they chose to terminate the test due to pain/discomfort, or they reached a maximum of 20 minutes of walking.

Total distance and time spent walking were recorded. Length duration times were recorded to allow for walking speed calculations for each length walked, which were used in the calculation energy cost during each length. Pain intensity and RPE were also assessed at the end of each length as participants rounded the cone. VO2 consumption was recorded using the single breath format, and then averaged for each 20 meter interval. Data from the first 1.5 minutes of collection was discarded to ensure the participant reached physiologic steady state. The energy cost of walking was

calculated by dividing VO2 consumption by average gait speed (as shown in the formula above) for the lengths contained within the following time windows during the walking test:

1. Early Stage Walking: For both groups, this was defined as the first usable minute (1.5-2.5 minute mark) after steady state was achieved. This represented the energy cost of walking measure during minimal pain intensity for the group with CLBPR, as pain intensity generally increased with duration of walking.

2. Late Stage Walking: For the group with CLBPR, this was defined as the energy cost of walking during the first full minute after maximal pain intensity was achieved. Use of this time point, as opposed to the last usable minute, helped isolate the effect that pain intensity hand on energy cost, as later minutes may have represented performance deterioration due to fatigue. For pain-free control group, this stage was defined as the last usable minute; in other words, if the full test was completed, the 19-20 minute mark was used.

Percent change in the energy cost of walking was calculated by using the following formula:

$$\frac{Late\ Stage - Early\ Stage}{Early\ Stage} * 100$$

3.2.3.1 Secondary Outcomes

Walking speed, RPE, and pain intensity ratings were averaged for the lengths contained within both early and late stages of walking. Furthermore, the total distance walked was calculated for both groups, and the time to reach maximal pain intensity was calculated for the CLBPR group.

3.2.4 Group Designation

After data collection was completed, participants with CLBPR were categorized based on whether their pain increased by the established minimal clinically important difference (MCID) during the walking test.[105] If participants with CLBPR experienced an increase of at least 2 points on the numeric pain rating scale during the 20-minute energy cost test, they were classified as achieving a clinically meaningful change in pain (CLBPR+MCID), otherwise they were classified as not achieving a clinically meaningful change in pain (CLBPR-MCID). The pain-free control participants that were matched to individuals in the CLBPR+MCID group were designated as Control Group A. The pain-free control participants that were matched to those in the CLBPR-MCID group were designated as Control Group B.

3.2.5 Statistical Analysis

Statistical analyses were performed using SPSS 24 (SPSS, Inc. Armonk, NY). One participant with CLBPR did not walk long enough to take late stage walking energy cost of walking measurements; neither they, nor their matched control participant was included in these analyses. Another participant did not have a change in pain during the entire walking test; hence, the late stage energy cost of walking measure was defined as the last usable minute of data. Descriptive analyses were performed for both CLBPR groups and both control groups, which included demographic characteristics, diabetes status, and pain-related disability; descriptive analyses were also conducted for the secondary outcomes. The repeated measures data violated the assumptions of parametric testing, hence a Related-Samples Wilcoxon Signed Rank test was used to determine within-groups differences of the energy cost of walking between early and late stages of walking for each group, separately. Linear

regression was used to examine the relationship between change in pain intensity and change in the energy cost of walking among those with CLBPR+MCID. Percent change in the energy cost of walking was designated as the dependent variable. Age,[54] body mass index,[106] and diabetes status[107] were entered into the first step as known covariates. Then, pain intensity rating from the early stage of walking was entered to control for baseline pain intensity. Finally, pain intensity rating from the late stage of walking was entered. For all analyses, α=.050.

3.3 Results

Participant demographics are provided in Table 3.1. Approximately 65% of those with CLBPR experienced a clinically meaningful increase in pain during the walking test. Both CLBPR groups were not statistically significantly different from their designated control groups on any of the demographic characteristics; however, it is worth noting that the CLBPR + MCID were clinically different from Control Group A on body mass index, with classifications of ‘obese’ and ‘overweight’, respectively.

Table 3.1: Descriptive characteristics

	CLBPR + MCID (n=13)	Control Group A (n=13)
	n (%)	
Female	8 (61.5)	8 (61.5)
Diabetic	3 (23.1)	3 (23.1)
	Mean (SD)	
Age (years)	69.2 (5.6)	70.2 (6.2)
BMI	33.1 (9.0)	27.4 (3.3)
Duration of LBP (years)	12.2 (15.8)	-
Duration of Leg Pain (years)	2.9 (3.8)	-
Quebec (0-100%)	43.2 (13.3)	-
	CLBPR – MCID (n=7)	**Control Group B (n=7)**
	n (%)	
Female	3 (42.9)	3 (42.9)
Diabetic	2 (28.6)	2 (28.6)
	Mean (SD)	
Age (years)	68.3 (2.3)	65.7 (3.2)
BMI	28.6 (7.7)	29.0 (5.3)
Duration of LBP (years)	16.4 (14.4)	-
Duration of Leg Pain (years)	6.3 (7.0)	-
Quebec (0-100%)	21.5 (13.0)	-

*p≤.050

Abbreviations: CLBPR = Chronic low back pain with radiculopathy; +MCID = experienced clinically important change in pain; -MCID = did not experience clinically important change in pain; BMI = Body Mass Index; LBP = low back pain; Quebec = Quebec Disability Index

Table 3.2 describes the secondary outcomes of all groups on the walking test. It is important to note that CLBPR+MCID group experienced approximately a 3.7 point increase in pain intensity, while the CLBPR-MCID group experienced less than a 1 point increase. Compared to matched participants in Control Group A, individuals with CLBPR+MCID walked shorter distances (mean difference = 446.9m, p<.001), walked slower in both stages of the test (early stage mean difference = .24 m/sec,

p<.001; late stage mean difference = .37 m/sec, p<.001), and reported higher perceived exertion in the late stage of the walking test (mean difference = -3.9, p=.001). These differences were not seen in the comparison between the CLBPR-MCID group and Control Group B.

Table 3.2: Secondary outcomes descriptive analysis

	CLBPR +MCID (n=13)	Control Group A (n=13)	p-value
	n (%)		
Walked full 20-minute duration	10 (76.9)	13 (100)	.066
	Mean (SD)		
Distance walked (m)	966.8 (219.7)	1413.7 (174.2)	<.001*
Early Stage Walking Speed (m/sec)	.91 (.10)	1.14 (.15)	<.001*
Late Stage Walking Speed (m/sec)	.83 (.19)	1.20 (.16)	<.001*
Early Stage RPE (6-20)	8.3 (1.8)	7.2 (.9)	.070
Late Stage RPE (6-20)	13.1 (2.8)	9.5 (2.3)	.001*
Early Stage Pain Intensity (0-10)	2.7 (1.1)	-	-
Late Stage Pain Intensity (0-10)	6.4 (1.8)	-	-
Time to reach max pain intensity (sec)	701.1 (187.5)	-	-
	CLBPR –MCID (n=7)	**Control Group B (n=7)**	**p-value**
	n (%)		
Walked full 20-minute duration	6 (85.7)	7 (100)	.299
	Mean (SD)		
Distance walked (m)	1165.7 (430.8)	1302.9 (149.6)	.442
Early Stage Walking Speed (m/sec)	1.04 (.16)	1.05 (.09)	.855
Late Stage Walking Speed (m/sec)	1.04 (.15)	1.13 (.17)	.334
Early Stage RPE (6-20)	8.7 (2.4)	7.9 (.8)	.379
Late Stage RPE (6-20)	10.4 (2.9)	10.86 (2.0)	.730
Early Stage Pain Intensity (0-10)	2.5 (1.2)	-	-
Late Stage Pain Intensity (0-10)	3.4 (1.3)	-	-
Time to reach max pain intensity (sec)	403.4 (310.1)	-	

*p≤.050

Abbreviations: CLBPR = chronic low back pain with radiculopathy; +MCID = experienced clinically important change in pain; -MCID = did not experience clinically important change in pain; RPE = rating of perceived exertion

Table 3.3 displays the results of the Related-Samples Wilcoxon Signed Rank test for within-group differences in energy cost between the early and late stages of walking. The CLBPR+MCID group had a significant increase in energy cost from early to late stages of walking, while the CLBPR-MCID and both control groups did not experience a significant change in energy cost.

Table 3.3: Within-group changes in the energy cost of walking

	Early Stage Energy Cost ($ml*kg^{-1}*m^{-1}$)	**Late Stage Energy Cost ($ml*kg^{-1}*m^{-1}$)**	
	Median (SIQR)		**p-value**
CLBPR + MCID	.211 (.028)	.214 (.039)	.006*
Control Group A	.190 (.015)	.189 (.015)	.807
CLBPR – MCID	.219 (.026)	.204 (.029)	.236
Control Group B	.181 (.025)	.181 (.016)	.735

*p≤.050
Abbreviations: SIQR = semi-interquartile range; CLBPR = chronic low back pain with radiculopathy; +MCID = experienced clinically important change in pain; -MCID = did not experience clinically important change in pain

Table 3.4 displays the results from the linear regression analysis, which examined the relationship between change in pain intensity and the change in the energy cost of walking for those who met the minimally clinically important difference (i.e. ≥2 points) for change in pain intensity. Late stage pain intensity was a significant contributor (p=.040) to the variance explained in percent change of the energy cost of walking, after controlling for potential covariates and early stage pain intensity. Although the assumptions of linear regression were met, one outlier was removed due to its influence on the regression characteristics. The difference between retaining and removing the outlier can be viewed graphically in Figure 3.1. Ultimately,

removing the outlier reduced the unique contribution of late stage pain intensity to the explanation of the variance in percent change in energy cost of walking from 47.2% (p=.027) to 41.2% (p=.040), after controlling for potential covariates and early stage pain intensity. Regardless, the statistical significance from the contribution of late stage pain intensity was preserved.

Table 3.4: Relationship between percent change in energy cost and pain intensity severity (adjusted for age, body mass index, and diabetes presence) with one outlier removed

Model	Independent Variables	R^2 Change	Adjusted R^2	p-change
1	Age, BMI, Diabetes Presence	.217	-.077	.558
2	Model 1 + Early Stage Pain Intensity	.010	-.215	.771
3	Model 2 + Late Stage Pain Intensity	.412	.338	.040*
*Unstandardized β (p-value) for Late Stage Pain Intensity: 6.14 (.040)**				

*p≤.050
Abbreviations: BMI = body mass index

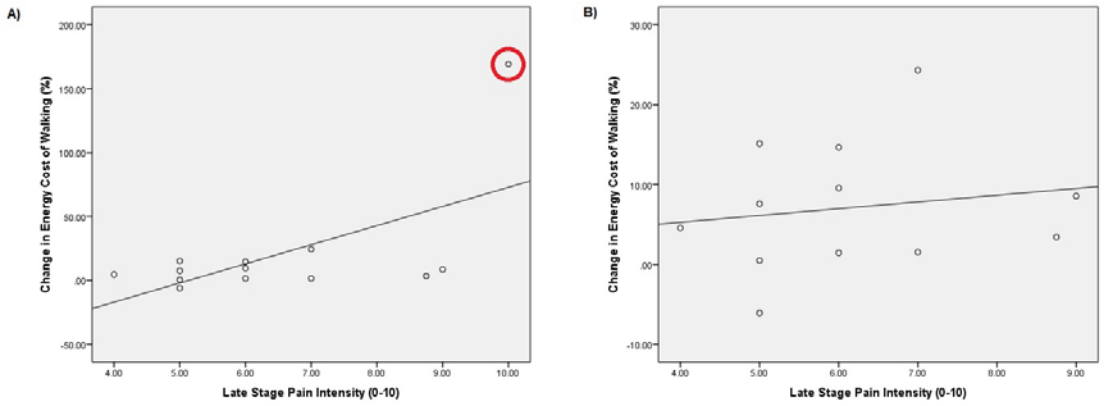

Figure 3.1: A) Graphically displays the unadjusted relationship between late stage pain intensity and percent change in energy cost with the outlier retained (circled in red), while B) displays the same relationship with the outlier removed. Note the difference in values on the y-axes.

3.4 Discussion

In this study, we evaluated the impact that acute pain provocation had on energy efficiency of walking in older adults with CLBPR, through the use of a pain-provocation model. The results suggest that clinically relevant increases in pain intensity drive increases in energy cost of walking in older adults with CLBPR. Furthermore, after controlling for covariates and early stage pain intensity, late stage pain intensity significantly contributed to the explanation of change in energy cost variance. Specifically, the regression slope coefficient suggests that for every one point increase in maximal pain intensity, there is a 6% increase in the energy cost of walking, for those who had a clinically significant change in pain intensity during walking. This work agrees with the findings from previous studies; provocations of experimentally-induced[50] and clinical pain[52] have been shown to drive increases in metabolic activity. Prior work has shown that CLBPR is associated with significant changes in gait,[108,109] which may drive energy inefficiency.

The clinical implications of this work are significant. Given that energy efficiency of walking is emerging as a strong predictor of future mobility decline,[27-29,46] these findings may help to shed some light on the physiological mechanisms behind the mobility limitations that are so commonly seen in older adults with different chronic pain conditions. Specifically, this work suggests that acute exacerbations of pain in those with CLBPR should be mitigated in order to prevent increases in the energy cost of walking. Although the recommendation that clinicians should focus on interventions that minimize pain provocation in those with CLBPR may not be a new recommendation, the physiological implications were previously unknown. In light of this work, it may be important to focus on pain reduction during

mobility tasks, such as walking, in order to preserve energy efficiency of movement, thereby reducing the risk of mobility decline.

One may point out that these energetic inefficiencies may be transient, as they occur only when pain is provoked. However, the true concern is when these acute-on-chronic episodes persist, forcing maladaptive gait mechanics. After long periods of time, these maladaptive mechanics may evolve into learned movement patterns, regardless of the presence of pain. Potential evidence for this phenomenon exists within other age-related chronic pain populations. For example, among individuals with knee osteoarthritis, total knee arthroplasty yields great reductions in pain intensity, but mobility remains limited.[71,72] This suggests that despite the removal of painful stimuli, impairments remain that may contribute to energy inefficiency. These impairments are likely unique to each chronic pain condition. Future research should validate this phenomenon, and identify the potentially modifiable impairments that may contribute to energy inefficiency in those with CLBPR.

This study has limitations. For instance, psychosocial factors are proposed to play a significant role in pain-related disability.[21] It is possible that psychoscocial factors may have a unique interaction with physiological measures; future research should elucidate the nature of these potential relationships. Furthermore, kinematic motion analysis was not feasible due to the nature of the methodology of this study; motion analysis may reveal specific kinetics and kinematics that drive energy inefficiency. Finally, to avoid confounding, this study excluded many older adults with CLBPR for comorbid conditions and severely limited mobility; this allowed for a unique insight into the physiology of pain and walking. However, comorbid conditions are common among those with CLBPR.[110] Regardless, we suspect that, in a

more inclusive sample, greater comorbidity burden (i.e. poorer health) may actually exacerbate the impact that pain provocation has on the energy cost of walking. These results need to be replicated in a larger, more inclusive sample of older adults with CLBPR.

3.5 Conclusion

Among older adults with CLBPR, acute pain provocation while walking, drives energy inefficiency. Higher severity of pain intensity contributes to greater energy inefficiency among older adults with CLBPR. Clinicians may focus on effective pain management strategies during walking to enhance energy efficiency, thereby decreasing the risk of future deterioration in mobility.

Chapter 4

GERIATRIC CHRONIC LOW BACK AND RADICULAR LEG PAIN: EXAMINING THE STRUCTURE OF WALKING ACTIVITY AND INACTIVITY

4.1 Introduction

Chronic low back pain with radiculopathy (CLBPR) is common among older adults,[6,85] given its link to age-related degenerative processes of the spine. It has been estimated that 47% of people over the age of 60 have lumbar spinal stenosis,[111] a condition that often manifests clinically as CLBPR.[85] CLBPR can lead to a host of mobility deficits, particularly affecting different aspects walking.[6,90,91,93] Walking limitations, such as speed reductions, are predictive of disability[11,12] and mortality[14,15] in older adults; these limitations are a hallmark of CLBPR, thus increasing the risk of poor health outcomes for individuals with this condition.

It is commonly thought that chronically painful conditions, such as CLBPR, lead to the deterioration of mobility through a pathway of physical inactivity and deconditioning.[21,22] In addition, physical inactivity is a key step in the proposed conceptual framework, the Pain-Energy Model, which posits that chronically painful conditions lead to physical inactivity by way of energy expenditure impairments.[89] The poor health outcomes associated with physical inactivity are indisputable and well known. Indeed, older adults with chronically painful conditions exhibit reductions in physical activity.[56,57] Approximately 4-13% of individuals with CLBPR meet the 2008 Physical Activity Guidelines set forth by the World Health Organization (i.e.

approximately 150 or more minutes of moderate-to-vigorous activity per week).[92] In comparison to pain-free age- and sex-matched pain-free peers, older adults with CLBPR take significantly less total steps per day.[91]

Although measuring daily step counts and fidelity to exercise recommendations can provide useful insight to the impact that CLBPR has on physical activity levels, these measures do not provide information on the *specific structure* of daily activity. Investigating specific walking activity deficits can provide important information, beyond the clinical setting.[61,112,113] Prior research has provided useful information on the amount of time that older adults with CLBPR spend in lighter intensity activities,[92] but more work needs to be done. In the CLBPR literature, we have little understanding of how often a person with this condition engages in walking, the duration of each bout of activity, and the distribution of different activity bout characteristics. Furthermore, to our knowledge, there appears to be no information regarding the inactivity patterns of these individuals. This could prove useful to clinicians, because sedentary behavior is proving to be an independent risk factor for negative health outcomes[114-119]; if this is a problem in those with CLBPR, clinicians could target this behavior in patient education and goal setting.

The purpose of this study was to address these gaps in the research literature using accelerometer-based step activity monitors. Our primary focus was to describe and compare the activity patterns of older adults with and without CLBPR, beyond just total steps counts. We hypothesized that older adults with CLBPR who experience a clinically meaningful increase in pain intensity with walking, would exhibit specific deficits in the distribution of their walking activity structure (i.e. distribution of steps/walking bout and cadence/walking bout) that would not be captured by total step

counts alone, compared to older adults with CLBPR who do not experience a clinically meaningful increase in pain with walking and older adults who are pain-free. Furthermore, we hypothesized that individuals with CLBPR who do experience a clinically meaningful increase in pain, would exhibit reduced activity and greater inactivity in summary characteristics of physical activity (e.g. total walking bouts per day, total inactive bouts per day, average steps per day, etc), compared to individuals with CLBPR who do not experience a significant increase in pain while walking and pain-free individuals.

4.2 Methods

4.2.1 Participants

This study was a comparative analysis of a sample of community-dwelling, cognitively intact (Folstein Mini-Mental State Exam score ≥ 18)[94] older adults with and without CLBPR. For the purposes of this study, the age group was defined as 60-85 years old. Participants with CLBPR recruited for this study met the following pain criteria: low back pain intensity ≥3/10, pain frequency ≥4 days per week, pain duration ≥3 months, and pain that radiated into the legs (at, or below, the knee) with walking. Participants with pain were excluded if they had any of the following: non-mechanical low back pain symptoms (e.g. unrelenting night pain, lack of sensation in the groin and/or buttocks), severely limited mobility (i.e. needed an assistive device for testing), significant cardiovascular or cardiopulmonary disease, a progressive neurological disorder, or a terminal illness.

Pain-free older adults were included if they did not have low back pain within the year prior to participation, or any significant areas of pain in the 72 hours

preceding the study evaluation. Furthermore, they must have matched a CLBPR participant already enrolled in the study based on the following characteristics: age (± 5 years), sex, and diabetes status. These individuals were excluded for the same criteria as mentioned for older adults with CLBPR.

All participants were recruited from newspaper advertisements, local senior centers, health fairs, and local physician and physical therapy clinics. Seventy-eight people were screened, 36 were either excluded or not interested in participating, and 42 were enrolled in the study. As previously mentioned, participants from the CLBPR and pain-free groups were matched based on age (± 5 years), sex, and diabetes status. For these analyses, however, all participants who had valid activity monitoring data (see subsection 4.2.4.1, Data Processing, for validity criteria) were analyzed, regardless if one of the two participants in the matched-pair were lacking activity data. Four participants with CLBPR and one control participant (n=5) did not have valid activity monitoring data; ten participants with CLBPR who experienced a clinically relevant increase in pain, seven participants with CLBPR who did not experience a clinically relevant increase in pain, and twenty control participants were included in these analyses (n=37). All policies and procedures were followed in accordance with the proposal approved by the University of Delaware Institutional Review Board and the Helsinki Declaration of the World Medical Association. All participants signed an informed consent form, and consent forms were securely stored.

4.2.2 Demographics and Self-Ratings

Participants reported their age, sex, diabetes status, and duration of both low back and leg pain. Height and weight were measured with the participant's shoes off using a Healthometer Professional™ digital scale (Mohawk Medical, Utica, NY), and

body mass index was calculated. The numeric pain rating scale[96] was used to measure worst pain intensity in the last 24 hours in both low back and leg(s), with anchors from 0 (“no pain”) to 10 (“worst possible pain”).

4.2.3 Group Designation

Participants completed a self-selected speed walking test, wherein they were instructed to walk in closed corridor, around two cones separated by 20 meters, for as long as possible or until they reached the 20-minute mark. During this time, pain intensity was measured every 20-meters. This test has been described in full detail in Chapter 3 (page 42, subsection 3.2.4, ‘Group Designation’). For this study, control participants were assigned to a single group. Participants with CLBPR were categorized after data collection was completed, based on whether their pain intensity increased by the established minimal clinically important difference (MCID) of ≥ 2 points.[105] If participants with CLBPR experienced an increase of at least 2 points on the numeric pain rating scale during the 20-minute energy cost of walking test, they were classified as achieving a clinically meaningful change in pain (CLBPR+MCID), otherwise they were classified as not achieving a clinically meaningful change in pain (CLBPR-MCID).

4.2.4 Activity Monitoring

Using Modus (Washington, DC) Step Activity Monitor 3™ (SAM) devices, free-living physical activity was measured by step activity monitoring, which is a performance-based measure of societal participation. SAM units have been shown to have good test-retest reliability and criterion validity.[120,121] The SAM unit was placed above the right ankle, just proximal to the lateral malleolus. The SAM unit was

calibrated to each participant's height, weight, and age. Storti et al have found SAM units to be accurate at a range of walking speeds, when holding the default settings constant for community-dwelling older adults.[122] Specifically, 'no' was selected for the *quick stepping* option; 'normal' was selected for *walking speed and leg motion* settings; and, 'uses moderate range of speeds' was selected for the *range of speeds* setting. The monitor was programmed to record data in 10-second intervals for a maximum of 8 days.

Participants were instructed to wear the monitor for seven full, consecutive days during all waking hours except during 'wet' activities, such as bathing and swimming. Standard instructions were given in a packet, as well as physical activity diaries to record the hours that the SAM unit was worn.

4.2.4.1 Data Processing

The SAM data were processed using a custom-designed Python program (Python Software Foundation, https://www.python.org) that was inspired from previous work.[61] First, all walking and inactive bouts were identified based on previously established definitions.[112] The start of a walking bout was defined as two or more subsequent 10-second intervals where steps occurred; the end of a walking bout was defined as a 10-second window of time where no steps occurred.[112] A single bout of inactivity was defined as the time in between walking bouts. If an inactive bout exceeded 180 minutes, it was considered as "non-wear time"[123] and was excluded from the analysis. If a participant did not have 10 hours of wear time during a day, then that day was considered invalid.[123,124] Four valid days were required to include a participant in the analysis,[125] and any valid days beyond the first four valid days were

excluded; this allowed for all participants to contribute a similar amount of valid wear time to the analysis.

4.2.4.2 Quintile Distribution of Steps/Bout and Cadence/Bout for Activity Structure

For walking bouts, the Python program adjoined sequential steps and time intervals to determine the duration of each walking bout (in seconds) and the number of steps taken during that bout, respectively. From this information, the cadence (steps/minute) for each bout was calculated. Since the SAM unit records information in strides (i.e. every step taken with the right leg only), the number of strides were doubled, as it is assumed that there was a sequential step with the leg without the activity monitor attached; this is consistent with previous literature.[112] The frequency distributions from the entire sample (i.e. all three groups together) were computed for the following physical activity characteristics: steps/walking bout and cadence/walking bout. The boundaries of each quintile were identified for both of these physical activity characteristics. For each of the individuals in each of the three groups, the number of active walking bouts that fell within each quintile was computed for each participant as raw counts and percent of total active bouts. Group means for each quintile were calculated.

4.2.4.3 Summary Characteristics of Physical Activity

Walking bouts were determined using the method described in the preceding section. To determine the length of inactive bouts, the Python program adjoined all sequential time intervals that were not contained in an active bout. Summary characteristics were calculated from the data collected over the four days: median walking bout duration, median steps/bout, median cadence/bout, and median inactive

bout duration. Median values were used for these variables, because the distribution of each characteristic had a heavy positive skew. Summary characteristics were also calculated for total number of walking bouts/day, total number of inactive bouts/day, average steps/day, average time spent walking/day, average time spent inactive/day, average percent of active wear time spent walking/day.

4.2.5 Statistical Analysis

Statistical analyses were performed using SPSS 24 (SPSS, Inc. Armonk, NY). Descriptive analyses were performed for both groups, including demographic characteristics, diabetes status, average pain intensity, and self-selected walking speed. To test the between-group differences in number of bouts and percent of total bouts, a 5x3 mixed-design analysis of covariance (ANCOVA) approach was used. The steps per walking bout quintiles were the within-group factor; the between-groups factor was the group designation (i.e. Control, CLBPR-MCID, CLBPR+MCID), and body mass index was designated as a covariate. This analysis was then repeated with the quintiles based on cadence/walking bouts. The quintile by group interaction effect was investigated to see if the quintile distributions differed between groups. Additionally, one-way between subject ANCOVAs were performed to compare summary characteristic variables among groups, while controlling for differences in body mass index. For all analyses, α=.050.

4.3 Results

Descriptive characteristics are provided in Table 4.1. As previously mentioned, participants were matched on age (±5 years), sex, and diabetes status. The groups differed significantly in body mass index (p=.006).

Table 4.1: Descriptive characteristics

	Controls (n= 20)	CLBPR-MCID (n=7)	CLBPR+MCID (n=10)
		n (%)	
Female	12 (57.1)	3 (42.9)	8 (61.5)
Diabetic	5 (23.8)	2 (28.6)	3 (23.1)
		Mean (SD)	
Age	68.5 (5.5)	68.3 (2.3)	70.1 (5.8)
BMI*	27.8 (4.2)	28.6 (7.7)	35.8 (8.2)
Duration of LBP (years)	-	16.4 (14.4)	14.8 (17.3)
Duration of Leg Pain (years)	-	6.3 (7.0)	3.3 (4.2)
Worst LBP Intensity in Past 24 Hours (0-10)	-	4.7 (1.8)	6.6 (2.6)
Worst Leg Pain Intensity in Past 24 Hours (0-10)	-	4.3 (2.4)	6.7 (2.5)

*p<.050 for full model
Abbreviations: CLBPR = Chronic low back pain with radiculopathy; +MCID = experienced clinically important change in pain; -MCID = did not experience clinically important change in pain; BMI = body mass index; LBP = low back pain;

Table 4.2 summarizes the results from the distribution analysis to identify the edges of each quintile for steps/bout and cadence/bout.

Table 4.2: Distribution analysis to identify quintiles for steps/bout and cadence/bout (n=37)

	Quintile Ranges (lower boundary – upper boundary)	
Quintile	**Steps per bout**	**Cadence per bout (steps/min)**
Q1	≤ 10.0	≤ 28.0
Q2	10.0 – 18.0	38.0 – 36.0
Q3	18.0 – 32.0	36.0 – 48.0
Q4	32.0 – 62.0	48.0 – 60.0
Q5	≥ 62.0	≥ 60.0

There was no significant difference among groups across quintiles for the number and percent of active bouts that fell within the different steps/walking bout quintile. There were significant interaction effects found for the number (p=.016) and percent p=.006) of active bouts that fell within the different cadence/walking bout quintile distributions, see Figure 4.1.

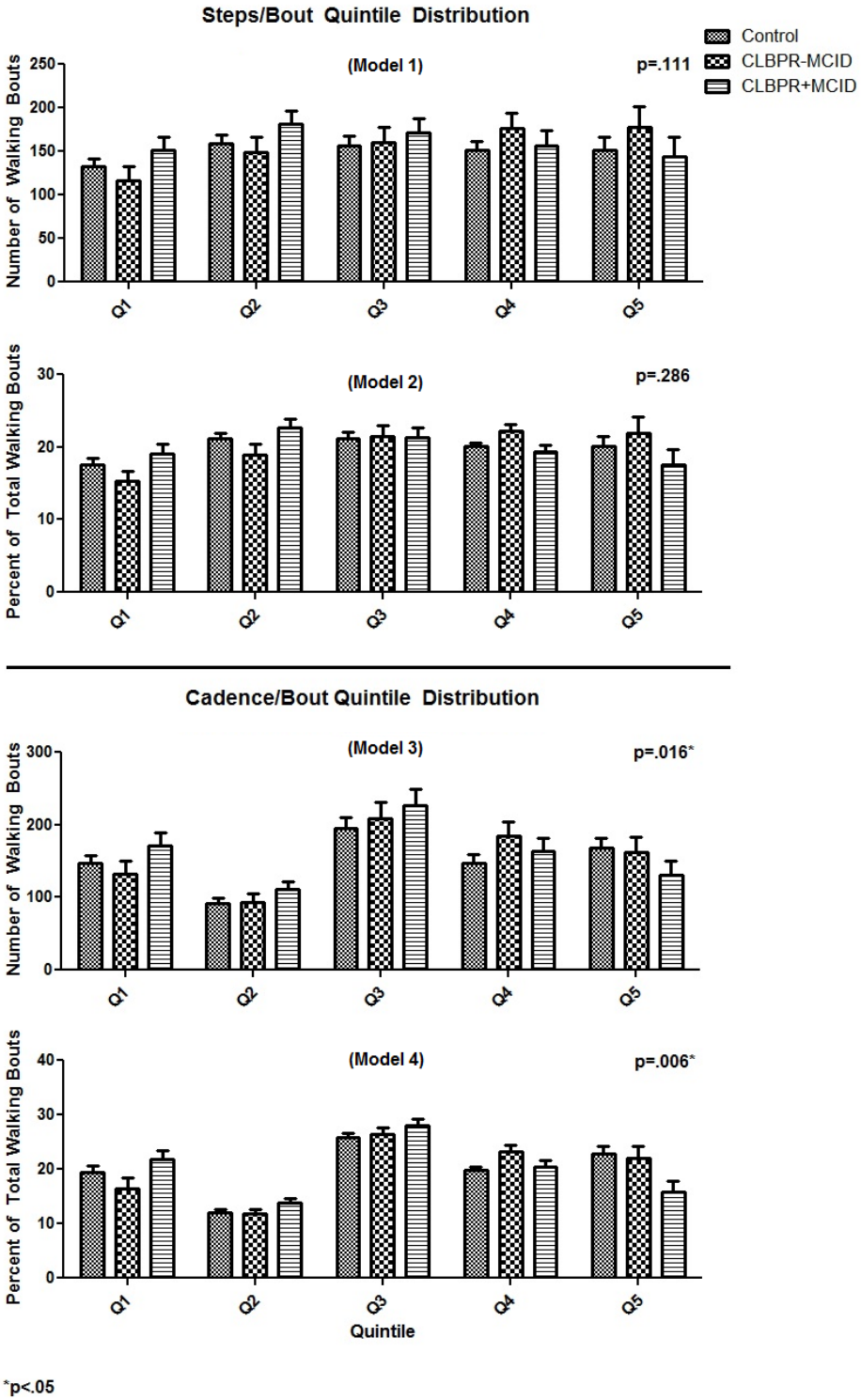

Figure 4.1: Differences in group quintile distributions for steps/bout and cadence/bout

Table 4.3 summarizes the mean and standard error values, adjusted for body mass index, for the number and percent of active bouts that for the cadence/walking bout quintiles.

Table 4.3: Means and standard error values, adjusted for body mass index, for the quintile distributions of Cadence/Bout

	Controls	CLBPR-MCID	CLBPR+MCID
Quintiles	**Adjusted Mean (SE)**		
	Number of Walking Bouts		
Q1	146.8 (11.1)	131.5 (18.1)	171.9 (16.9)
Q2	91.7 (6.9)	93.6 (11.3)	111.5 (10.5)
Q3	196.0 (14.3)	208.1 (23.4)	227.1 (21.7)
Q4	147.4 (11.9)	184.0 (19.5)	164.0 (18.1)
Q5	168.3 (12.8)	162.9 (20.8)	130.7 (19.4)
	Percent of Total Walking Bouts		
Q1	19.5 (1.15)	16.5 (1.87)	21.8 (1.74)
Q2	12.0 (0.52)	11.8 (0.84)	13.8 (0.78)
Q3	25.9 (0.74)	26.4 (1.21)	28.1 (1.13)
Q4	19.8 (0.76)	23.2 (1.24)	20.4 (1.15)
Q5	22.9 (1.30)	22.1 (2.12)	15.9 (1.97)

Abbreviations: Abbreviations: CLBPR = Chronic low back pain with radiculopathy; +MCID = experienced clinically important change in pain; -MCID = did not experience clinically important change in pain; SE = Standard Error

Table 4.4 summarizes the results of the various one-way ANCOVAs, adjusting for body mass index. The between-group differences in median walking bout duration (p=.087), median steps/bout (p=.064), and median cadence/bout (p=.121) approached statistical significance. The between-group differences in the total number of active bouts, total number of inactive bouts, average steps/day, average time spent walking/day, average time spent inactive/day, and average percent of wear time spent walking/day, were not statistically significant. When the means were unadjusted for

body mass index, the CLBPR+MCID group differed significantly from the Control group in average steps/day (p=.009), average time spent walking/day (p=.038), and average percent of wear time spent walking per day (p=.028). In addition, the CLBPR+MCID group differed significantly from the CLBPR-MCID group in median walking bout duration (p=.005) and median steps/bout (.011).

Table 4.4: Between-group differences in physical activity summary statistics, adjusted for body mass index

	Control	CLBPR -MCID	CLBPR +MCID		
	Adjusted Mean (SE)			Partial Eta Squared	p-value
Median walking bout duration (sec)	35.7 (1.2)	39.7 (2.0)	33.3 (1.9)	.137	.087
Median Steps/Bout	23.8 (1.2)	28.0 (1.9)	21.6 (1.8)	.154	.064
Median Cadence/bout (steps/min)	42.1 (0.9)	44.3 (1.6)	39.6 (1.5)	.120	.121
Median inactive bout duration (sec)	44.3 (2.4)	42.9 (3.9)	42.9 (3.6)	.004	.930
Total Walking Bouts/Day	187.6 (11.4)	195.0 (18.7)	201.3 (17.3)	.013	.810
Total Inactive Bouts/Day	151.9 (8.5)	153 (13.9)	164.4 (12.9)	.018	.739
Avg Steps/Day	9974 (761)	9775 (1244)	8374 (1158)	.036	.548
Avg Time Spent Walking/Day (min)	179.4 (12.2)	191.6 (20.0)	174.1 (18.6)	.013	.808
Avg Time Spent Inactive/Day (min)	645.3 (19.8)	685.9 (32.4)	649.4 (30.2)	.035	.551
Avg Percent of Wear Time Spent Walking/Day	21.9 (1.4)	21.8 (2.3)	21.0 (2.2)	.003	.945

*p≤.050

Abbreviations: Abbreviations: CLBPR = Chronic low back pain with radiculopathy; +MCID = experienced clinically important change in pain; -MCID = did not experience clinically important change in pain; SE = Standard Error; Avg = average

Table 4.5: Unadjusted between-group differences in physical activity summary statistics

	Control	CLBPR -MCID	CLBPR +MCID	p-value CON v. -MCID	p-value CON v. +MCID	p-value -MCID v. +MCID
		Mean (SD)				
Median walking bout duration (sec)	36.3 (4.8)	40.0 (5.8)	32.0 (6.3)	.125	.051	.005*
Median Steps/Bout	23.9 (3.8)	28.0 (6.4)	21.5 (5.8)	.066	.216	.011*
Median Cadence/bout (steps/min)	41.8 (3.5)	44.1 (4.6)	40.6 (5.2)	.218	.466	.099
Median inactive bout duration (sec)	42.0 (9.5)	41.4 (12.2)	48.5 (15.3)	.913	.163	.231
Total Walking Bouts/Day	199.3 (48.4)	202.9 (94.5)	172.3 (40.6)	.890	.234	.289
Total Inactive Bouts/Day	161.0 (35.9)	159.0 (69.8)	142.1 (33.6)	.918	.267	.432
Avg Steps/Day	10649.7 (3624.2)	10223.2 (5101.7)	6709.9 (2520.6)	.794	.009*	.062
Avg Time Spent Walking/Day (min)	193.2 (57.0)	200.78 (96.7)	140.0 (14.7)	.787	.038*	.061
Avg Time Spent Inactive/Day (min)	631.8 (96.2)	676.9 (103.1)	682.6 (69.6)	.269	.160	.900
Avg Percent of Wear Time Spent Walking/Day	23.5 (7.0)	22.9 (11.3)	16.9 (4.7)	.839	.028*	.113

*p≤.050; Abbreviations: CON = control; CLBPR = chronic low back pain with radiculopathy; +MCID = experienced clinically important change in pain; -MCID = did not experience clinically important change in pain; SD = standard deviation; Avg = average

4.4 Discussion

In this study, we sought to determine the impact that CLBPR had on the structure of walking activity among older adults. We hypothesized that older adults with CLBPR who experience a clinically relevant increase in their symptoms while walking, would experience deficits in the structure and summary measures of their walking activity. Our results suggest that the quintile distribution of cadence/bout differs based on pain status; older adults with CLBPR who experience a clinically relevant increase in their symptoms, have less bouts and spend a smaller proportion of their walking bouts in higher cadence walking. Because cadence is a component of walking speed, this suggests that this group walks slower in real-world activity; this corroborates our earlier findings that older adults with CLBPR who experience clinically relevant increases in their symptoms, walk slower under clinical conditions (see Chapter 3). This is clinically relevant, because having a slower cadence increases the risk of experiencing a meaningful decline in walking speed in the future.[126] Furthermore, if we had compared groups on only median cadence/bout, this finding would have been missed, as the between-groups comparison of this measure was not statistically significant (p=.121).

However, we failed to detect any between-group differences in the distribution of steps/bout quintiles. In addition, the differences in summary physical activity characteristics were not statistically significant between-groups to the extent that we hypothesized. Although it is possible that CLBPR may not have an impact on the level of physical activity in the geriatric population, prior work has shown that older adults with CLBPR take significantly less steps per day than healthy control participants,[91] a finding that conflicts with our results. If differences do exist between these two groups, we may have failed to detect it for two reasons.

First, our study had stringent inclusion and exclusion criteria for participation; people with major comorbid disease and severe mobility limitations were excluded, leaving a relatively health segment of older adults with CLBPR. This was noticeable in the difference in our results compared to that of Winter et al. They found that those with CLBPR, on average, took approximately 7,128 steps/day (3,564 gait cycles/day)[91] compared to participants in the CLBPR-MCID group who, on average, took approximately 10,223 steps/day; however, the CLBPR+MCID group average (6,710 steps/day) was much closer to that of Winter et al.

Second, the difference in body mass index between our groups was stark, requiring mathematical control for this potential covariate. For example, once the means for average steps/day were adjusted for body mass index, the group averages were very similar to one another (Control = 9974, CLBPR-MCID = 9775, CLBPR+MCID = 8374 steps/day). Furthermore, if we did not adjust for body mass index, between-group differences would have existed between Control and CLBPR+MCID groups for average steps/day, average time spent walking/day, and average percent of wear time spent walking/day ($p \leq .05$).

Although the findings of this study are limited, they still have potentially important clinical implications. Older adults with CLBPR who experience a clinically relevant increase in symptoms during walking, experience deficits in cadence/bout activity. In general, it appears that this group of individuals walks slower than those with CLBPR who do not experience a clinically relevant increase in pain, or their pain-free peers. This a potential deficit that may need to be addressed in this patient population, given the link between walking speed and adverse health outcomes in older adults.[12,14,15]

4.5 Conclusion

The structure of physical activity characteristics may be impacted by the presence of CLBPR in older adults, particularly in the realm of step cadence; these findings are novel, as analyses like this have not been performed in older adults with CLBPR. However, the relatively healthy nature of this sample and the stark differences in body mass index may have limited the findings of this study. Future research should repeat these methods in a more inclusive, larger cohort of older adults with CLBPR.

Chapter 5

EXAMINING THE RELATIONSHIP BETWEEN ENERGETIC EFFICIENCY AND DAILY PHYSICAL ACTIVITY AMONG OLDER ADULTS WITH CHRONIC LOW BACK AND RADICULAR LEG PAIN

5.1 Introduction

Chronic low back pain with radiculopathy (CLBPR) is common among older adults,[6,85] given its link to age-related degenerative processes of the spine. CLBPR can detrimentally impact mobility,[6,93] thereby increasing the difficulty of real-world walking.[6] Recently, there has been work to support that this condition has a profound effect on daily activity levels, as measured by step activity monitoring.[90-92]

It is commonly thought that chronically painful conditions, such as CLBPR, lead to a deterioration of mobility through a pathway of physical inactivity.[21,27,29] Indeed, low physical activity predicts the development and progression of disability among older adults.[127-130] Yet our understanding of the potentially modifiable factors that drive physical activity level is poor, particularly in those with CLBPR. Psychosocial factors, such as fear-avoidance, have been found to contribute to physical activity levels in some chronic pain populations, but this evidence also suggests that this psychosocial impairment only partially contributes to physical inactivity,[58,131,132] indicating that there are other factors that may drive physical activity behavior. Once identified, these potentially modifiable factors can be targeted through interventions to improve this important outcome. In the proposed conceptual framework, the Pain-Energy Model, energy inefficiency is hypothesized to drive

reductions in physical activity, thereby leading to reduced energy capacity and mobility limitations.[89]

Energy efficiency of walking has not only been identified as a strong predictor of mobility deterioration among older adults,[28,29,46] but also as an important contributor to physical activity in other mobility-limited patient populations.[59,62] Danks et al found that higher energy cost of walking was tightly linked to the less steps per day taken by individuals who had a stroke[62]; Maltais et al found similar results among people with cerebral palsy.[59] However, it is unknown if energy inefficiency is linked to reduced physical activity among older adults with CLBPR. Furthermore, as established in Chapter 2, energy efficiency declines as pain is provoked, but it is unclear if these changes in energy cost of walking are relevant in explaining physical activity levels among older adults with CLBPR. It is important to gain a better understanding of this relationship, because energy efficiency is potentially modifiable; specific rehabilitative interventions have been shown to be effective in improving energy efficiency of walking, among community-dwelling older adults.[74,75]

Although untested in those with CLBPR, this relationship appears logical; if those with CLBPR have worse energy efficiency when pain is provoked, then they may be less inclined to walk, thereby reducing their physical activity and increasing their risk of mobility deterioration. The purpose of this study was to examine this relationship. We hypothesized that among older adults with CLBPR, greater increases in the energy cost of walking at self-selected speed, would be more strongly related to reduced walking activity and greater inactivity, as measured by accelerometry. Furthermore, we hypothesized that provocation-status of their symptoms would

moderate this relationship, such that this relationship would be stronger (i.e. more greatly reduced physical activity levels for each unit increase in the change in the energy cost of walking), among those with highly provocative symptoms.

5.2 Methods

5.2.1 Participants

This study was a comparative analysis of a sample of community-dwelling, cognitively intact (Folstein Mini-Mental State Exam score ≥ 18)[94] older adults with CLBPR. For the purposes of this study, the age group was defined as 60-85 years old. Participants recruited for this study met the following pain criteria: low back pain intensity ≥3/10, pain frequency ≥4 days per week, pain duration ≥3 months, and pain that radiated into the legs (at, or below, the knee) with walking. Participants with pain were excluded if they had any of the following: non-mechanical low back pain symptoms (e.g. unrelenting night pain, lack of sensation in the groin and/or buttocks), severely limited mobility (i.e. needed an assistive device for testing), significant cardiovascular or cardiopulmonary disease, a progressive neurological disorder, or a terminal illness.

All participants were recruited from newspaper advertisements, local senior centers, health fairs, and local physician and physical therapy clinics. Fifty-seven people were screened, 36 were either excluded or not interested in participating, and 21 were enrolled in the study. Four participants were not included in the analysis; three participants did not have valid activity monitor data (see subsection 5.2.5.1, Data Processing, for validity criteria), and one participant had neither complete energy cost of walking data nor valid activity monitor data. Seventeen older adults with CLBPR

were included in this analysis: ten participants with CLBPR whose symptoms were highly provocative, and seven participants whose symptoms were not provoked (n=17). All policies and procedures were followed in accordance with the proposal approved by the University of Delaware Institutional Review Board and the Helsinki Declaration of the World Medical Association. All participants signed an informed consent form, and consent forms were securely stored.

5.2.2 Demographics and Self-Ratings

Participants reported their age, sex, diabetes status, and duration of both low back and leg pain. Height and weight were measured with the participant's shoes off using a Healthometer Professional™ digital scale (Mohawk Medical, Utica, NY), and body mass index was calculated. The numeric pain rating scale[96] (0-10) was used to measure pain intensity, with anchors from 0 ("no pain") to 10 ("worst possible pain"), during the energy cost of walking test (see test protocol below).

5.2.3 Energy Cost of Walking

The energy cost of walking, which is the amount of energy consumed per unit of distance, was measured using metabolic gas analysis equipment. The energy cost of walking (mL/kg/min) was derived by using the following formula:

$$Energy\ Cost\ of\ Walking = \frac{Average\ VO2}{Walking\ Speed} = \frac{mL\ O2/kg\ body\ weight/min}{meters/min}$$

The energy cost of walking at self-selected speed has been used to measure energetic efficiency in other studies.[27,28,46] Prior work has shown that the most energetically efficient walking speed for healthy, older adults occurs close to their normal self-selected pace.[54]

In this study, the energy cost of walking was assessed by measuring oxygen (VO2) consumption (mL/kg/min) during a walking test, conducted at the participant's self-selected speed around a marked course with a known distance. The testing protocol was adapted from a similar study in peripheral arterial disease patients by Gardner et al.[52] The test was conducted in a closed corridor, as participants walked back and forth around two traffic cones that were separated by 20 meters. Participants were instructed to walk at their usual, comfortable pace until they chose to terminate the test due to pain/discomfort, or they reached a maximum of 20 minutes of walking.

Total distance and time spent walking were recorded. Length duration times were recorded to allow for walking speed calculations for each length walked, which were used in the energy cost calculation during each length. Pain intensity and RPE were also assessed at the end of each length as participants rounded the cone. Oxygen consumption was recorded using the single breath format, and then averaged for each 20 meter interval. Data from the first 1.5 minutes of collection was discarded to ensure the participant reached physiologic steady state. The energy cost of walking was calculated by dividing VO2 consumption by average gait speed (as shown in the formula above) for lengths contained within the following time windows during the walking test:

3. Early Stage Walking: This was defined as the first usable minute (1.5-2.5 minute mark) after steady state was achieved. This represented the energy cost of walking measure during minimal pain intensity, as pain intensity generally increased with duration of walking.

4. Late Stage Walking: This was defined as the energy cost of walking during the first full minute after maximal pain intensity was achieved. One participant did not have a change in pain intensity during the walking test, so this time point was defined as the last usable minute of data (19-20 minute mark).

5.2.4 Group Designation (Provocation Status)

Participants were categorized after the energy cost of walking test was completed, based on whether their pain increased by the established minimal clinically important difference (MCID) of ≥ 2 points,[105] during the self-selected walking test. If participants with CLBPR experienced an increase of at least 2 points on the numeric pain rating scale during the 20-minute energy cost test, meaning they were highly provocative, they were classified as achieving a clinically meaningful change in pain (CLBPR+MCID). Otherwise, participants were classified as not achieving a clinically meaningful change in pain (CLBPR-MCID), as their symptoms were not highly provocative.

5.2.5 Activity Monitoring

Using Modus (Washington, DC) Step Activity Monitor 3™ (SAM) devices, free-living physical activity was measured by step activity monitoring, which is a performance-based measure of societal participation. SAM units have been shown to have good test-retest reliability and criterion validity in community-dwelling older adults.[120,121] The SAM unit was placed above the right ankle, just proximal to the lateral malleolus. The SAM unit was calibrated to each participant's height, weight, and age. Storti et al have found SAM units to be accurate at a range of walking speeds, when holding the default settings constant.[122] Specifically, 'no' was selected for the *quick stepping* option; 'normal' was selected for *walking speed and leg motion* settings; and, 'uses moderate range of speeds' was selected for the *range of speeds* setting. The monitor was programmed to record data in 10-second intervals for a maximum of 8 days.

Participants were instructed to wear the monitor for seven full, consecutive days during all waking hours except during 'wet' activities, such as bathing and swimming. Standard instructions were given in a packet, as well as physical activity diaries to record the hours that the SAM unit was worn.

5.2.5.1 Physical Activity Outcomes

The SAM data were processed using a custom-designed Python program (Python Software Foundation, https://www.python.org) that was inspired from previous work.[61] First, all walking and inactive bouts were identified based on previously established definitions.[112] The start of a walking bout was defined as two or more subsequent 10-second intervals where steps occurred; the end of a walking bout was defined as a 10-second window of time when no steps occurred.[112] A single bout of inactivity was defined as the time in between walking bouts. If an inactive bout exceeded 180 minutes, it was considered as "non-wear time"[123] and was excluded from the analysis. If a participant did not have 10 hours of wear time during a day, then that day was considered invalid.[123,124] Four valid days were required to include a participant in the analysis,[125] and any valid days beyond the first four valid days were excluded; this allowed for all participants to contribute a similar amount of valid wear time to the analysis.

For walking bouts, the Python program adjoined sequential steps and time intervals to determine the duration of each walking bout (in seconds) and the number of steps taken during that bout, respectively. From this information, the cadence (steps/minute) for each bout was calculated. Since the SAM unit records information in strides (i.e. every step taken with the right leg only), the number of strides were doubled, as it is assumed that there was a sequential step with the leg without the

activity monitor attached; this is consistent with previous literature.[112] To determine the length of inactive bouts, the Python program adjoined all sequential time intervals that were not contained in an active bout. Physical activity outcomes were calculated: median walking bout duration, median steps/bout, median cadence/bout, and median inactive bout duration. Median values were used for these variables, because the distribution of each characteristic had a heavy positive skew. The following summary statistics were also calculated as physical activity outcomes: total number of walking bouts/day, total number of inactive bouts/day, average steps/day, average time spent walking/day, average time spent inactive/day, average percent of wear time spent walking/day.

5.2.6 Statistical Analysis

Statistical analyses were performed using SPSS 24 (SPSS, Inc. Armonk, NY). Descriptive analyses were performed for the sample, including demographic characteristics, diabetes status, pain intensity characteristics, energy cost of walking, and physical activity outcomes. The relationships between the energy cost of walking and physical activity outcome variables were tested using linear regression. Separate physical activity outcomes were entered as the dependent variables for each model. In the first step, age, diabetes status, and body mass index were entered into the regression model as potential covariates. Then, early stage energy cost of walking was entered into the model to control for baseline energy cost. Next, the main effects for late stage energy cost of walking and group designation were entered into the model. Finally, the late stage energy cost of walking by group designation interaction term was entered into the model. For all analyses, α=.050.

5.3 Results

Descriptive characteristics are provided in Table 5.1. The groups did not differ on sex, diabetes status, age, or body mass index. The groups did not differ significantly on energy cost of walking measures for either stage of the walking test. Expectedly, those in the CLBPR+MCID group had a greater late stage pain intensity value (p=.003) compared to those in the CLBPR-MCID group, but did not differ in pain intensity for the early stage of walking. Those with CLBPR+MCID also took longer to achieve maximal pain intensity (p=.010). For physical activity measures, those in the CLBPR+MCID group had a shorter median walking bout duration (p=.018) and took less steps per walking bout (p= .047), compared to those in the CLBPR-MCID. The groups did not differ significantly on other physical activity outcomes.

Table 5.1: Descriptive characteristics

	CLBPR+MCID (n=10)	**CLBPR-MCID (n=7)**
	n (%)	
Female	5 (50.00)	3 (42.86)
Diabetic	2 (20.00)	2 (28.57)
	Mean (SD)	
Age (years)	70.10 (5.82)	68.29 (2.29)
BMI	35.83 (8.15)	28.61 (7.72)
Early Stage Energy Cost of Walking ($ml*kg^{-1}*m^{-1}$)	.207 (.032)	.228 (.031)
Late Stage Energy Cost of Walking ($ml*kg^{-1}*m^{-1}$)	.251 (.098)	.222 (.031)
Early Stage Pain Intensity (0-10)	2.39 (0.85)	2.50 (1.22)

Table 5.1 continued.

Late Stage Pain Intensity (0-10)	6.10 (1.66)*	3.43 (1.27)*
Time to Reach Max Pain Intensity (sec)	741.50 (161.07)*	403.4 (310.11)*
Median Walking Bout Duration (sec)	32.00 (6.32)*	40.00 (5.77)*
Median Steps/Bout	21.50 (5.84)*	28.00 (6.43)*
Median Cadence/Bout (steps/min)	40.55 (5.22)	44.09 (4.57)
Median Inactive Bout Duration (sec)	48.50 (15.28)	41.43 (12.15)
Total Walking Bouts/Day	172.28 (40.60)	202.86 (94.52)
Total Inactive Bouts/Day	142.05 (33.60)	159.04 (68.83)
Avg Steps/Day	6709.85 (2520.63)	10223.21 (5101.75)
Avg Time Spent Walking/Day (min)	140.00 (46.56)	200.78 (96.73)
Avg Time Spent Inactive/Day (min)	682.60 (69.62)	676.91 (103.15)
Avg Percent of Wear Time Spent Walking/Day	16.90 (4.67)	22.87 (11.31)

*p≤.050

Abbreviations: CLBPR = Chronic low back pain with radiculopathy; +MCID = experienced clinically important change in pain; -MCID = did not experience clinically important change in pain; SD = Standard Deviation BMI = Body Mass Index; Avg = Average

Table 5.2 displays the results of the regression analyses. Neither change in energy cost of walking, nor the change in energy cost of walking by group interaction term, explained a significant proportion of the variance for any of the physical activity outcomes. However, the interaction term did approach significance for both median steps/bout (p=.055) and median cadence/bout (p=.139).

Table 5.2: Relationships between change in energy cost of walking and physical activity outcomes, adjusted for body mass index, diabetes, and early stage walking energy cost of walking

Model	R^2 Change	Adjusted R^2	p-change	R^2 Change	Adjusted R^2	p-change
	DV = Median Walking Bout Duration			**DV = Total Inactive Bouts/Day**		
1	.206	.093	.198	.367	.277	.041*
2	.251	.277	.102	.022	.185	.811
3	.021	.242	.519	.000	.111	.974
4	.028	.211	.466	.047	.098	.381
	DV = Median Steps/Bout			**DV = Avg Steps/Day**		
1	.084	-.047	.542	.422	.340	.022*
2	.193	.036	.242	.081	.337	.405
3	.088	.076	.242	.023	.311	.479
4	.204	.310	.055	.010	.258	.647
	DV = Median Cadence/Bout			**DV = Avg Time Spent Walking/Day**		
1	.010	-.132	.935	.487	.413	.009*
2	.171	-.092	.320	.033	.359	.672
3	.032	-.145	.517	.011	.317	.625
4	.162	.000	.139	.006	.259	.718
	DV = Median Inactive Bout Duration			**DV = Avg Time Spent Inactive/Day**		
1	.665	.617	<.001*	.453	.374	.015*
2	.020	.579	.694	.042	.327	.617
3	.022	.574	.378	.118	.438	.094
4	.039	.594	.241	.003	.387	.781
	DV = Total Walking Bouts/Day			**DV = Avg Percent of Wear Time Spent Walking/Day**		
1	.379	.290	.036*	.549	.485	.004*
2	.024	..204	.788	.025	.432	.712
3	.003	.135	.831	.000	.381	.973
4	.053	.133	.346	.006	.329	.703

Model 1 = BMI, Diabetes
Model 2 = Model 1 + Early Stage Energy Cost, Group
Model 3 = Model 2 + Change in Energy Cost
Model 4 = Model 3 + Change in Energy Cost x Group Interaction
*p≤.050
Abbreviations: DV = Dependent Variable; BMI = Body Mass Index; Avg = Average

5.4 Discussion

In this study, we examined the potential relationship between the change in the energy cost of walking (i.e. energy efficiency) and physical activity outcomes among older adults with CLBPR. We hypothesized the relationship would be stronger among older adults with CLBPR who experienced a clinically relevant increase in pain intensity while walking, compared to those who did not experience this change in pain. In other words, we posited that greater increases in the energy cost of walking would be related to reductions in physical activity, particularly among those with CLBPR who had significant increase in pain during walking. Ultimately, our results did not support our hypotheses, but posed some interesting preliminary findings.

The interaction term between group assignment and change in the energy cost of walking was not statistically significant for any of the physical activity outcomes; however, it approached significance for median steps/bout (p=.055) and median cadence/bout (p=.139), suggesting that this relationship may exist, but this study was statistically underpowered to detect it. Using G*Power (version 3.1.9.2),[133] we conducted a post-hoc power analysis to determine the sample size needed for statistical significance in these regression models. For median steps/bout, a total sample size of 34 would be needed to find an R^2 value of .204 statistically significant ($\alpha = .05$, power = .80). For median cadence/bout, a total sample size of 43 would be needed to find an R^2 value of .162 statistically significant ($\alpha = .05$, power = .80). This suggests that relationships may exist in this population, but the effect size is smaller than originally anticipated, and we did not originally power for two separate groups with CLBPR.

In addition to being underpowered, our study has other limitations. First, the findings conflict with other studies published on the physical activity levels of those

with CLBPR. Winter et al found that those with CLBPR took approximately 7,128 steps/day,[91] as referenced in the previous chapter. Those with CBLPR who experienced a clinically relevant increase in pain intensity took a similar amount of steps/day on average compared to the sample in the study by Winter et al[91]; however, those that did not experience a clinically relevant increase in pain during walking were strikingly more active. This suggests that a portion of our sample was much more mobile than what has been previously described in the literature. Indeed, our testing procedures required our participants to have a high level of mobility, resulting in a highly mobile subgroup of the older adult CLBPR population. Furthermore, we excluded individuals based on many significant comorbid conditions (e.g. peripheral vascular disease, chronic obstructive pulmonary disease, neurological conditions, etc), leaving a relatively healthy sample of individuals with CLBPR. Thus, these findings can only be limited to this highly mobile, healthy segment of the geriatric CLBPR population. We expect that if these analyses were repeated in a more representative sample of the geriatric CLBPR population (i.e. less mobile and greater comorbid disease burden), these relationships may be stronger.

Regardless, there were still strengths of this study that should be noted. This approach to analyzing physical activity data was novel. Typically, many studies explore the nature of physical activity through average steps/day only; however, there is important clinical information that can be gained from observing many components of the structure of physical activity.[61,112,113] Our results suggest that change in the energy cost of walking may still be potentially related to these components, which was not necessarily observed by examining the relationship between change in energy cost of walking and average steps/day alone.

5.5 Conclusion

Among older adults with CLBPR, greater increases in the energy cost of walking may be related to specific aspects of physical activity, such as steps taken per walking bout and cadence of a walking bout, but these findings failed to reach statistical significance. Because this study was underpowered and the inclusion/exclusion criteria were, perhaps, too restrictive, these analyses should be repeated in a larger, more generalizable sample of older adults with CLBPR.

Chapter 6

ENERGETIC EFFICIENCY AS A PREDICTOR OF REDUCED ENERGY CAPCITY IN THE BALTIMORE LONGITDUINAL STUDY OF AGING: THE MODERATING ROLE OF LUMBOPELVIC PAIN SEVERITY

6.1 Introduction

In the geriatric population, low back and hip pain often coincide with one another,[134-137] affecting the lumbopelvic and femoroacetabular regions of the body. The prevalence of hip osteoarthritis is more than 20% higher among older adults with low back pain compared to those without low back pain.[138] In addition, many of those with symptomatic hip osteoarthritis, report concurrent symptoms in their low back.[137] Among older adults, chronic lumbopelvic pain (LPP) conditions (e.g. chronic low back pain, hip osteoarthritis), hereafter defined as pain in the hip or low back regions, are linked to greater disability and reduced quality of life.[6,7,10,139,140] Decreases in walking speed are a hallmark sign of the disablement process, and they are predictive of disability[12-14] and mortality[15] in the geriatric population; older adults with chronic LPP have a tendency to walk slower than their pain-free peers,[7,10,17,20,141] but the reason why this occurs is not exactly clear.

With age, energy efficiency of movement declines,[28,36,54] raising the energetic cost of walking, while the maximum amount of energy able to be expended decreases (i.e. reduced energy capacity).[31] Recently, experts in gerontology research have shown convincing evidence that age-related declines in walking speed may be due, in part, to the combination of energetic inefficiency in the presence of reduced energetic

capacity.[29,46] Schrack et al hypothesized that energy inefficiencies may drive reductions in energy capacity, by way of physical inactivity.[29] However, to our knowledge, the longitudinal nature of the relationship between energy efficiency and energy capacity has not been investigated among older adults.

Furthermore, painful conditions appear to have an important impact on energy efficiency and capacity. Ko et al found that older adults with knee pain have less energetically efficient gait than those without knee pain.[51] Gussoni et al found that the presence of painful hip joint impairments are linked to a higher energy cost of walking.[53] In terms of energy capacity, Smeets et al have found that those with chronic low back pain have reductions in the energy capacity compared to those without pain.[65,66] In the Pain-Energy Model, it is hypothesized that pain has a unique impact on the relationship between energy efficiency and changes in energy capacity, which are not seen in those who are pain-free (i.e. moderation effect).[89] However, this phenomenon has not been studied among older adults with LPP, nor has it been studied longitudinally in any geriatric pain population. If such a relationship does exist, then energy efficiency of movement would be a particularly important rehabilitation target in the disability pathway; currently, interventions aimed at energy efficiency are not commonplace in the rehabilitation of geriatric LPP conditions.

The purpose of this study was two-fold. Using data from a large, population-based study of older adults, the Baltimore Longitudinal Study of Aging (BLSA), we 1) sought to determine the extent to which energy efficiency predicted changes in energy capacity over time among older adults, and 2) explored the potential moderation effect that LPP severity might have on the relationship between energy efficiency and capacity. We hypothesized that among older adults, higher energy cost of walking at

self-selected speed (i.e. worse energy efficiency) would be predictive of decreases in Peak Walking VO2 (i.e. worse energy capacity) after controlling for potential covariates, regardless of LPP presence. We also hypothesized that LPP severity would modify the relationship between the energy cost of walking at self-selected speed and Peak Walking VO2 in older adults with LPP, such that the relationship would be stronger in those with severe LPP, compared to individuals with mild-to-moderate LPP.

6.2 Methods

The BLSA is a study on human aging, established in 1958 and supported by the National Institute of Aging Intramural Research Program. A general description of the study has been published previously.[142] The BLSA is a prospective cohort study, conducted in Baltimore, MD, that continuously enrolls community-dwelling volunteers that are free of major disease or impairment at the time of enrollment; participants undergo a comprehensive health and functional screening assessment every 1-4 years for the rest of their lives. Participants who are aged 60-79 years have a follow-up evaluation every two years, whereas those who are aged ≥ 80 years have one every year. Data include, but are not limited to, interview questions regarding pain presence and duration, as well as energy expenditure measurements.

6.2.1 Participants

This secondary analysis consists of BLSA volunteers aged ≥ 60 years who reported no difficulty walking ≥1/4 mile and participated in energy expenditure measures for two consecutive visits (visit 1 = baseline, visit 2 = follow-up). The energy expenditure assessment was fully implemented in September 2007, and data up

until December 2014 were used in these analyses. Of the 1,186 participants who were of the appropriate age at the time of the baseline visit, 340 participants had complete data for these analyses; all other participants were either missing some or all of the data required for this study. At baseline, individuals who were not eligible for these analyses were older (75.4 vs 72.2 years, p<.001), had a slightly higher body mass index (27.4 vs 26.7, p=.038), demonstrated a higher energy cost of walking at self-selected speed (.174 vs .168 mL/kg/meter, p=.025), and had a lower Peak Walking VO2 (16.5 vs 17.7 mL/kg/min, p=.001) compared to those included in these analyses; those not eligible were also more likely to have a past medical history of stroke (4.5% vs 0.6%, p=.001) and spinal stenosis (8.1% vs. 4.8%, p=.048). The Internal Review Board of the National Institute of Environmental Health Sciences approved the study protocol, and all participants provided written informed consent.

6.2.2 Demographics and Anthropometrics

All participants completed a health history interview and physical examination. Height and weight were measured according to standard protocols, and body mass index was calculated.

6.2.3 Group Designation

Based on their response to interview questions during their baseline visit, participants were assigned to one of three groups: no pain, mild-to-moderate LPP, and severe LPP. Participants were first asked, “In the past year, have you had any low back pain?” If the participant responded ‘yes,’ they were asked rate their “usual back pain over the past year from 0-10, where 0 indicates ‘no pain’ and 10 indicates ‘extremely intense pain’. The middle of the scale was used as a cut-point for

classification: those that responded with scores from ≤ 5 were classified as having ‘mild-to-moderate low back pain’, and those that responded with a score of ≥ 6 were classified as having ‘severe low back pain’. Participants were then asked, “In the past 12 months, have you had pain in or around either hip on most days, for at least one month?” If a participant responded ‘yes’, they were asked to rate their hip pain as either ‘mild’, ‘moderate’, ‘severe’, or ‘extreme’. Those that responded with ‘mild’ or ‘moderate’ were classified as having ‘mild-to-moderate hip pain’, and those that responded with ‘severe’ or ‘extreme’ were classified as having ‘severe hip pain’. Participants were assigned to groups based on the most severe rating of the two bodily regions: if participants had neither low back nor hip pain, they were assigned to the ‘no pain’ group; if their most severe rating of the two regions was ‘mild-to-moderate’, they were assigned to the ‘mild-to-moderate LPP’ group; if their most severe rating of the two regions was ‘severe’, they were assigned to the ‘severe LPP’ group.

6.2.4 Energy Cost of Walking

Energy cost of walking (mL/kg/m) was assessed at the baseline visit using a portable metabolic gas analysis device (Cosmed k4b^2) during 2.5 minutes of overground walking at self-selected speed; this test was the warm-up component of the modified long distance corridor walk test. The Cosmed k4b^2 device was calibrated before use with reference gases and a 3.0 liter syringe for gas flow. The course set-up and test protocol were identical to those mentioned in earlier chapters; participants were instructed to walk back and forth around two traffic cones separated by 20 meters at the “usual comfortable pace” in a continuous loop. The participant was instructed to stop after 2.5 minutes.

The Cosmed k4b^2 unit continuously measured oxygen consumption for each breath and averaged these measures over 30-second intervals. Energy expenditure was calculated as the average volume of oxygen (VO2) consumed per kilogram of body weight per minute (mL/kg/min). To calculate average VO2 consumption for the test, the first 1.5 minutes of data were discarded to allow for the participant to reach physiologic steady state, and the remaining one-minute average was used. Gait speed was determined by measuring the total distance walked divided by 2.5 minutes. Then, to measure the amount of oxygen consumed per kilogram of body weight *per meter walked* (mL/kg/meter), energy cost of walking was calculated by normalizing average oxygen consumption to gait speed, as described in earlier chapters.

6.2.5 Peak Walking VO2

At baseline and follow-up visits, Peak Walking VO2 was assessed during the 400-meter segment of the long-distance corridor walk test, which is a validated measure of cardiorespiratory fitness in older adults.[70] The course set-up and test protocol were identical to the Peak Walking VO2 test described in earlier chapters. Using the same course as the energy cost test, participants were instructed to "walk as fast as possible, at a pace you can sustain for 400 meters." Standardized encouragement was given with each lap, as well as the number of laps remaining.

The Cosmed k4b^2 device was used to measure VO2 consumption during this test, and it remained on the participant for 2 minutes following the completion of the test to ensure adequate breath collection. To calculate Peak Walking VO2 (mL/kg/min), data from the first 1.5 minutes were discarded to allow the participant to reach physiologic steady state. Then, the remaining readings from the test were averaged to arrive at a single measure of average VO2 consumption, Peak Walking

VO2. Percent change in Peak Walking VO2 from baseline to follow-up visit, was calculated using the following formula:

$$\frac{Follow\ Up\ Peak\ Walking\ VO2 - Baseline\ Peak\ Walking\ VO2}{Baseline\ Peak\ Walking\ VO2} * 100$$

6.2.6 Statistical Analysis

Statistical analyses were performed using SPSS 24 (SPSS, Inc. Armonk, NY). Descriptive analyses were performed for the three LPP groups. Linear regression models were used to examine the potential relationship between baseline energy cost of walking and percent change in Peak Walking VO2, as well as the moderating effect that pain severity had on this relationship within those with LPP. In the first model, the entire sample was analyzed without grouping; percent change in Peak Walking VO2 was designated as the dependent variable. Age, sex, and body mass index were entered into the first step as suspected covariates. Then, baseline energy cost of walking was entered into the model. In the second regression model, only those with LPP (mild-to-moderate or severe) were analyzed; percent change in Peak Walking VO2 was, again, designated as the dependent variable. Age, sex, and body mass index were entered into the first step. Then, the main effects for baseline energy cost of walking and LPP group status (mild-moderate vs. severe) were entered into the model. Finally, the baseline energy cost of walking x LPP group interaction term was entered into the last step of the model. For all analyses, α=.050.

6.3 Results

Table 6.1 displays the descriptive characteristics for all groups. With increasing level of LPP severity, there appeared to be decreasing trend for age

($p<.001$) and an increasing trend for body mass index ($p=.011$). Groups did not differ on sex, energy cost of walking or Peak Walking VO2.

Table 6.1: Descriptive characteristics

	No LPP (n=194)	Mild-to-Moderate LPP (n=114)	Severe LPP (n=32)
		n(%)	
Female	87 (44.8)	56 (49.1)	20 (62.5)
		Mean (SD)	
Age (years)*	73.80 (8.31)	70.03 (7.92)	69.84 (7.65)
Body Mass Index*	26.16 (3.90)	27.40 (4.44)	28.01 (5.60)
Energy Cost of Walking (mL/kg/meter)	.166 (.033)	.170 (.031)	.172 (.025)
Peak Walking VO2 (mL/kg/min)	17.5 (4.02)	17.9 (3.79)	17.6 (5.16)

*p≤.050 for model
Abbreviations: LPP = Lumbopelvic Pain; SD = Standard Deviation

Table 6.2 displays the results from the linear regression analysis of the entire sample, which examined the relationship between baseline energy cost of walking and percent change in Peak Walking VO2, regardless of the presence of LPP. Potential covariates did not significantly explain the variance in the percent change in Peak Walking VO2. Baseline energy cost of walking accounted for 15.0% of the variance in the percent change in Peak Walking VO2 ($p<.001$). Four outliers were removed to satisfy the assumption of normality of residuals, leaving total n=336 for this analysis.

Table 6.2: Relationship between baseline energy cost of walking and percent change in Peak Walking VO2, adjusted for age, sex, and body mass index (n=366)

Model	Independent Variables	R^2 Change	Adjusted R^2	p-change
1	Age, Sex, BMI	.005	-.004	.638
2	Model 1 + Energy Cost of Walking	.150	.140	<.001*
Unstandardized β (p-value) for Energy Cost of Walking: -227.9 (≤.001)*				

†6 outliers removed
*p≤.050
Abbreviations: BMI = Body Mass Index

Table 6.3 displays the results from the linear regression analysis of only those with LPP, which examined the relationship between energy cost of walking and percent change in Peak Walking VO2, and the moderating effect that LPP severity had on this relationship. Potential covariates did not significantly explain the variance in percent change in Peak Walking VO2. Beyond the main effects for baseline energy cost of walking and group designation (mild-to-moderate vs. severe LPP), the interaction between these two factors explained an additional 5.2% of the variance in percent change in Peak Walking VO2 (p=.003). Unadjusted relationships from both regression models (Table 6.2 and 6.3) are displayed in Figure 6.1.

Table 6.3: Moderating effect of severe pain on the relationship between energy cost of walking and change in Peak Walking VO2 among those with LPP, adjusted for age, sex, and body mass index (n=146)

Model	Independent Variables	R^2 Change	Adjusted R^2	p-change
1	Age, Sex, BMI	.002	-.019	.951
2	Model 1 + Energy Cost of Walking and LPP Group	.169	.142	<.001*
3	Model 2 + Energy Cost of Walking x LPP Group Interaction Term	.052	.190	.003*
Unstandardized β (p-value) for Energy Cost of Walking: -186.8 (≤.001); Interaction: -361.2 (.003*)*				

*p≤.050

Abbreviations: BMI = body mass index, LPP = lumbopelvic pain

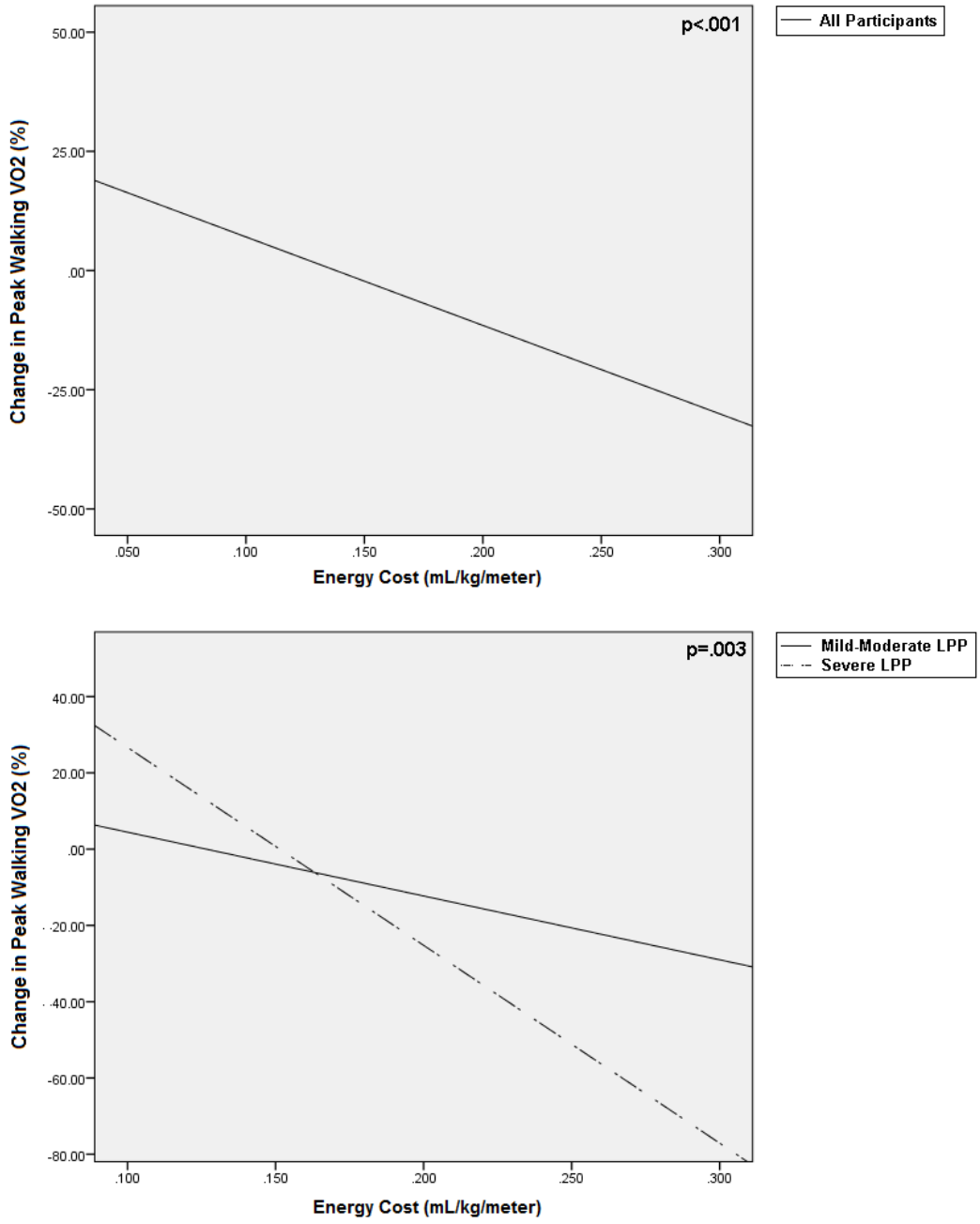

Figure 6.1: Graphical illustration of: 1) the unadjusted relationships between baseline energy cost of walking and percent change in Peak Walking VO2, regardless of LPP presence (top image); 2) the moderating effect of LPP severity in the unadjusted relationship between baseline energy cost of walking and percent change in Peak Walking VO2, among those with LPP (bottom image).

6.4 Discussion

The purpose of this study was to determine the potential impact that energy efficiency had on the change in energy capacity in community-dwelling older adults, regardless of the presence of LPP. In addition, we examined the potential moderation effect that LPP severity had on the relationship between these two energetic factors, among older adults with LPP. The slope coefficient for this regression model suggests that for every .01 mL/kg/meter increase in the energy cost of walking, Peak Walking VO2 declines by approximately 2.28%, among older adults (regardless of LPP presence). This suggests that the energy cost of walking at self-selected speed (i.e. energy efficiency) does, in fact, predict greater reductions in Peak Walking VO2 (i.e. energy capacity), among older adults. This relationship appears to be stronger among those with severe compared to mild-to-moderate LPP; the slope coefficient for this model indicates that, compared to individuals with mild-to-moderate LPP, those with severe LPP experience an *additional* decline in Peak Walking VO2 of approximately 3.61% (total decline of approximately 5.48%), for every .01 mL/kg/meter increase in baseline energy cost.

To our knowledge, this is the first study to establish a longitudinal link between energy efficiency and capacity among older adults. Prior models of disability development in older adults have suggested that energy inefficiency leads to declines in energy capacity. Schrack et al have suggested that greater energetic inefficiency with movement may result in one becoming more sedentary to avoid the increased metabolic exertion of daily tasks, which ultimately would drive reductions in energy capacity.[27,29] Although we did not investigate the role that physical inactivity has in this pathway in these analyses, this is the first study to lend support to the theory that energy inefficiency drives reductions in energy capacity over time.

In the Pain-Energy model, we have proposed that pain drives energy inefficiency, which, in turn, leads to diminished energy capacity.[89] In earlier chapters, we have shown that chronic low back pain with radiculopathy is linked to energy inefficiency (see Chapter 2), and that more severe forms of this condition result in greater deterioration of energy efficiency while walking for long periods of time (see Chapter 3). Similarly, our findings from this study suggest that LPP severity bears an influence on the pathway from energy inefficiency to diminished energy capacity. This study not only establishes the longitudinal nature of this relationship, but it also lends validity to the Pain-Energy Model in a different patient population, as our prior work focused only on older adults with chronic low back pain with radiculopathy.

This work has important clinical implications. Poor energy capacity has been shown to be risk factor for disability[23,24] and mortality[25,26]; identifying potentially modifiable risk factors for the decline energy capacity, such as energetic inefficiency, is important, so that interventions can be developed to target these factors. There is evidence to suggest the energy cost of walking is modifiable among older adults, through specific rehabilitation intervention that focus on the smoothness of gait (i.e. timing and coordination).[74,75] Although these types of interventions are generally not commonplace for older adults with LPP conditions, our results suggest that they may be effective when targeting key steps in the pathway to disability, such as reduced energy capacity. Further, our work suggests that energy inefficiency is a particularly important impairment that should be targeted among older adults with severe LPP.

It is important to note that, although there were limitations to this study, large-scale, prospective studies that contain these types of energy expenditure measurements are exceedingly rare. The prospective nature of this study allowed us to clarify the

temporal nature of these relationships. However, this study did have limitations. First, it is important to note that only a small proportion of the potentially eligible participants were able to be included in the analysis. The missing data analysis, provided in the Methods section, helps to shed light on why this occurred. In general, those who did not have full data were generally older and less healthy. These analyses required that participants walk at least 400-meters as quickly as possible at *both* time points; the demands of these tests may have been greater than many older adults can tolerate. Furthermore, having a diagnosis of lumbar spinal stenosis, which can manifest as LPP, was related to not having complete data for this study; this is a drawback, because lumbar spinal stenosis can contribute to low back pain, a core component of LPP. In reality, if older, less healthy individuals were included in this analysis, the relationships may have actually been *stronger* than what we observed. Second, although our analyses helped to establish the moderating effect of LPP severity on this longitudinal relationship, they did not identify which specific components of severe LPP contribute to this effect. Future studies should examine the components of LPP that should be targeted by intervention to mitigate this effect.

6.5 Conclusion

Among older adults, higher energy cost of walking (i.e. energy inefficiency) is predictive of greater reductions in Peak Walking VO2 (i.e. diminished energy capacity) over time, and this relationship is stronger among those with severe LPP when compared to mild-to-moderate LPP. Because prior work has shown that reduced energy capacity is predictive of disability and mortality, the energy cost of walking at self-selected speed should be a point of focus for intervention in all older adults, but particularly in those with severe LPP. Future work should examine the components of

severe LPP (e.g. psychosocial impairments, muscle weakness, impaired trunk muscle coordination) that contribute to the moderation effect seen in this relationship.

Chapter 7

SUMMARY

Mobility deteriorates with age, but these deficits are more pronounced in those with chronic musculoskeletal pain conditions. However, we are unsure of why these changes occur in older adults with chronic musculoskeletal pain conditions. Emerging evidence suggests that the age-related decline in walking speed is driven by energy inefficiency in the presence of diminished energy capacity. Chronically painful conditions may have an important impact on this metabolic pathway, but this is largely unexplored.

The goal of this work was to: 1) propose a new conceptual framework to enhance the understanding of the metabolic mechanisms behind the deterioration of mobility among those with pain; 2) test different aspects of this model among those with different pain conditions (e.g. chronic low back pain with radiculopathy and lumbopelvic pain); 3) provide insight as to the clinical implications that this new model possesses. The specific aims of this project are to determine whether:

AIM 1: Older adults with CLBPR have greater impairments in energy expenditure, and whether these impairments will worsen with pain provocation compared to pain-free older adults.

- Hypothesis 1.1: Older adults with CLBPR will have a greater energy cost of walking (i.e. energy inefficiency) during walking at self-selected speed, compared to pain-free, matched controls.

The energy cost of walking at self-selected speed was greater among older adults with CLBPR compared to matched, pain-free control participants. This suggests that CLBPR is linked to reduced energy efficiency among older adults, which, given previous research, may lead to greater reductions in walking speed. Decreased walking speed is predictive of disability and mortality. Therefore, energy efficiency may be an important, potentially modifiable factor to focus on in the rehabilitation of older adults with CLBPR.

- Hypothesis 1.2 Older adults CLBPR will achieve lower Peak Walking VO2 values during a fast-pace walking test of energy capacity, compared to pain-free, matched controls.

Peak Walking VO2 is reduced among older adults with CLBPR compared to matched, pain-free participants. Given the predictive nature of reduced Peak Walking VO2 in disability onset and mortality risk, this may be an important, potentially modifiable factor to target for intervention. In addition to findings from Hypothesis 1.1, these results lend validity to the chronic portion of the Pain-Energy Model: these results suggest that not only do chronic pain conditions influence energy efficiency, but they also contribute to reductions in energy capacity.

- Hypothesis 1.3 Higher energy cost of walking will be cross-sectionally related to Peak Walking VO2 after controlling for suspected covariates, but this relationship will be stronger among those with CLBPR.

No cross-sectional relationship was found between energy efficiency and capacity. Limitations in our study design may have prevented us from detecting a relationship. The small sample size in this study may have led to a lack of sufficient power to test this hypothesis. Furthermore, we assumed that energy cost of walking at *self-selected speed* was the best indicator of energy efficiency, based on previous

work; however, for those with CLBPR, we found that the energy cost of walking during the fast-speed, peak test of energy capacity was *lower* compared to the energy cost of walking at self-selected speed. This finding may have contributed the absence of a relationship between energy efficiency and capacity. Further work needs to be completed to investigate the hypothesized relationship between increased energy cost and reduced energy capacity seen in our Pain-Energy model.

- Hypothesis 1.4: Older adults with CLBPR, who exhibit a clinically meaningful increase in pain while walking, will have a greater energy cost of walking in late compared to early stages of walking, but this factor will remain unchanged in those who do not exhibit this change in pain intensity or are pain-free.

Older adults with CLBPR who experienced a clinically relevant increase in their pain did, in fact, have significant increase in their energy cost of walking from early to late stages of walking at self-selected speed. These changes were not observed among older adults with CLBPR group who did not reach a clinically relevant increase in their pain, nor were they seen in participants who were pain-free. This suggests that preventing pain from significantly rising in older adults with CLBPR, may prevent energy cost from rising in conjunction. These results also help to validate our Pain-Energy model, supporting the premise that the pain experiences drives energy inefficiency.

- Hypothesis 1.5 Among older CLBPR, who exhibit a clinically meaningful increase in pain, increases in pain intensity from early to late stages of walking, will be related to increases in the energy cost of walking.

Regression analyses suggested that increases in maximal pain intensity, contributed to reductions in energy efficiency, among older adults with CLBPR who experienced a clinically relevant increase in pain while walking. This suggests that

reducing the maximal pain intensity during ambulation will limit the increase in energy cost experienced during walking in this subgroup of older adults with low back pain. This finding supports the Pain-Energy model, suggesting that increases in the pain experience, yield proportional decreases in energy efficiency.

AIM 2: Older adults with CLBPR will demonstrate lower levels of physical activity and increased inactivity compared to pain-free older adults in a descriptive analysis of step activity monitoring.

- Hypothesis 2.1: Older adults with CLBPR who experience a clinically relevant increase in their pain with walking, will have a significantly different quintile distribution from those who do not experience a significant increase in their pain and pain-free peers, in the following daily physical activity structural characteristics:
    - Hypothesis 2.1a: steps per walking bout (raw bout count)
    - Hypothesis 2.1b: steps per walking bout (percent of total bouts)
    - Hypothesis 2.1c: average cadence per walking bout (raw bout count)
    - Hypothesis 2.1c: average cadence per walking bout (percent of total bouts)

Our findings partially supported these hypotheses. Older adults with CLBPR who experienced a clinically relevant increase in pain intensity while walking, had a significantly different quintile distribution for average cadence per walking out in both raw count *and* percentage of total bouts. These difference were most pronounced in the highest quintiles of average cadence per walking bout, suggesting that not only did they have less bouts in those high-cadence quintiles (i.e. decreased volume of activity), but the proportion of their total bouts that fell into those quintiles was much

less (i.e. difference in pattern of overall activity). We may have been underpowered to detect differences in the quintile distribution for steps per walking bout (raw bout count and percent of total bouts). Regardless, these findings do partially support our conceptual model in that CLBPR that is provoked with walking, is linked to reductions in certain aspects of physical activity.

- Hypothesis 2.2: Older adults with CLBPR who experience a clinically relevant increase in their pain with walking, will have reduced levels of activity compared to those who do not experience a significant increase in pain and matched, pain-free peers, in the following physical activity summary characteristics:
    - Hypothesis 2.2a: median walking bout duration
    - Hypothesis 2.2b: median steps per walking bout
    - Hypothesis 2.2c: median cadence per walking bout
    - Hypothesis 2.2d: median inactive bout duration
    - Hypothesis 2.2e: total walking bouts per day
    - Hypothesis 2.2f: total inactive bouts per day
    - Hypothesis 2.2g: average steps per day
    - Hypothesis 2.2h: average time spent walking per day
    - Hypothesis 2.2i: average time spent inactive per day
    - Hypothesis 2.2j: average percent of wear time spent walking per day

Our findings did not support these hypotheses. Although some of these findings approached statistical significance, none surpassed the threshold of $p \leq .050$. Study design limitations contributed to these null findings. Specifically, the sample had a relatively high level of mobility and were in good health due to the stringent exclusion criteria, and stark differences between-groups in body mass index, required

mathematical adjustment in our models. If these comparisons were unadjusted for body mass index, more statistically significant results would have been seen. Future research should repeat these analyses in a larger, more representative sample of older adults with CLBPR.

AIM 3: Deficits in energy efficiency are associated with decreased physical activity levels and increased inactivity in older adults with CLBPR, and these relationships will be moderated by the provocation status of their symptoms.

- Hypothesis 3.1: Among older adults with CLBPR, greater increases in the energy cost of walking at self-selected speed will be associated with the following:
    - Hypothesis 3.1a: lower median walking bout duration.
    - Hypothesis 3.1b: lower median steps per walking bout.
    - Hypothesis 3.1c: lower median cadence per walking bout.
    - Hypothesis 3.1d: higher median inactive bout duration.
    - Hypothesis 3.1e: less total walking bouts per day.
    - Hypothesis 3.1f: more total inactive bouts per day.
    - Hypothesis 3.1g: less average total steps per day.
    - Hypothesis 3.1h: less average time spent walking per day.
    - Hypothesis 3.1i: more average time spent inactive per day.
    - Hypothesis 3.1j: lower average percent of wear time spent walking per day.

Our findings did not support these hypotheses. The main effect for the change in energy cost of walking at self-selected speed from early to late stages, did not contribute to the variance explained in any of the listed physical activity measures;

however, the relationship for the main effect for change in energy cost and average time spent inactive per day did approach statistical significance. This indicates that while relationships may exist, we were underpowered to detect them. Again, we may also have failed to detect relationships due to the high level of mobility and good health our sample. Future research should repeat these analyses in a larger, more representative sample of older adults with CLBPR.

- Hypothesis 3.2: The relationships listed above are moderated by pain provocation status (i.e. experiences a clinically relevant increase in pain intensity during walking) of older adults with CLBPR.

Our findings did not support these hypotheses. The interaction between change in energy cost of walking and provocation status did not contribute to the variance explained in any of the listed physical activity outcome measures; however, the relationship for this interaction term and median steps per walking bout, as well as median cadence per walking bout, did approach statistical significance. This indicates that while relationships may exist, we were underpowered to detect them. Again, we may also have failed to detect relationships due to the high level of mobility and good health our sample. Future research should repeat these analyses in a larger, more representative sample of older adults with CLBPR.

AIM 4: Deficits in energetic efficiency are predictive of declines in energetic capacity over time, and if lumbopelvic pain intensity status will moderate this relationship, in a population-based study, the Baltimore Longitudinal Study of Aging.

- Hypothesis 4.1: Among older adults, higher baseline energy cost of walking will be predictive of declines in Peak Walking VO2 over time, regardless of the presence of lumbopelvic pain.

The energy cost of walking at baseline was predictive of the percent change in Peak Walking VO2 from baseline to follow-up in this large sample of community-dwelling older adults; this suggests that reduced energy efficiency is a risk factor for energy capacity decline. These findings also support the validity of our conceptual model, in that reductions in energy capacity are driven by energy inefficiency. Future research should investigate the longitudinal impact that interventions targeting energy efficiency, have on the change in Peak Walking VO2.

- Hypothesis 4.2: Pain intensity will moderate the relationship between higher baseline energy cost of walking and decline in Peak Walking VO2 among older adults with lumbopelvic pain, such that those with severe lumbopelvic pain will exhibit greater reductions in Peak Walking VO2 for each unit increase in the energy cost of walking.

The interaction effect between pain severity group and baseline energy cost of walking was significant in terms of explaining the variance of percent change in Peak Walking VO2. The negative slope coefficient suggests that for older adults with severe LPP, a one unit change in the energy cost of walking, yields a greater reduction in Peak Walking VO2 over time, compared to those with mild-to-moderate LPP. Not only does this support our Pain-Energy model in that greater pain experiences drive changes in this pathway, but it also suggests that the mitigation of LPP severity may attenuate the reduction in Peak Walking VO2 associated with energy inefficiency. Future studies should focus on interventions that may impact this pathway to see if they reduce disability.

7.1 Closing Remarks

This dissertation project has proposed a new conceptual model, the Pain-Energy Model, for understanding the physiological mechanisms that may drive the

deterioration of mobility in older adults with chronically painful conditions. In Chapters 2-6, we tested certain aspects of this conceptual model; broadly speaking, much of our data supported the hypotheses we posed. It appears that CLBPR does, in fact, influence important aspects of energy expenditure, including efficiency and capacity. Furthermore, our results suggest that the severity of the pain experience impacts this pathway. Future research may target these potentially relevant clinical impairments, in hopes of reducing the risk of disability onset and progression.

Our work, however, did not fully support our hypotheses regarding the importance of physical inactivity in our pathway. Limitations exist with regard to our sample that may have prevented us from optimally investigating this component of the conceptual model. Our sample, particularly those with CLBPR, did not only exhibit high levels of mobility and few comorbidities, but they were disparate on body mass index; individuals with CLBPR possessed much greater levels of body mass index, compared to their matched, pain-free peers. This is paradoxical, considering the relatively healthy nature of *both* groups. Furthermore, while we were appropriately powered to detect physiological differences between these groups, we may have been underpowered to detect significance in measures of broader constructs, such as daily activity in society. Future research is needed in a larger sample that is more representative of older adults with CLBPR.

In closing, we feel that this work produced results that warrant further investigation, given their clinical relevancy. Future studies should investigate the validity of this model in greater depth. For example, we did not conduct path analysis in this project; mediation analysis would help to identify the ordinal nature of the steps in this pathway. Further, future studies should design and test interventions centered

on the pathway proposed in this project; if these interventions prove effective in reducing disability, the clinical implications of this model would grow, and clinical practice would shift. As a result, older adults with chronic pain may enjoy a greater quality of life.

REFERENCES

1. International Association for the Study of Pain. Taxonomy. 2016; http://www.iasp-pain.org/Taxonomy. Accessed June 23, 2016.
2. Institute of Medicine (US) Committee on Advancing Pain Research C, and Education. *Relieving pain in America: A blueprint for transforming prevention, care, education, and research.* Washington, DC: National Institutes of Health;2011.
3. Helme RD, Gibson SJ. The epidemiology of pain in elderly people. *Clin Geriatr Med.* 2001;17(3):417-431, v.
4. Weiner DK, Kim YS, Bonino P, Wang T. Low back pain in older adults: are we utilizing healthcare resources wisely? *Pain Med.* 2006;7(2):143-150.
5. Bressler HB, Keyes WJ, Rochon PA, Badley E. The prevalence of low back pain in the elderly. A systematic review of the literature. *Spine (Phila Pa 1976).* 1999;24(17):1813-1819.
6. Hicks GE, Gaines JM, Shardell M, Simonsick EM. Associations of back and leg pain with health status and functional capacity of older adults: findings from the retirement community back pain study. *Arthritis Rheum.* 2008;59(9):1306-1313.
7. Hicks GE, Simonsick EM, Harris TB, et al. Cross-sectional associations between trunk muscle composition, back pain, and physical function in the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci.* 2005;60(7):882-887.
8. Onder G, Cesari M, Russo A, Zamboni V, Bernabei R, Landi F. Association between daily pain and physical function among old-old adults living in the community: results from the ilSIRENTE study. *Pain.* 2006;121(1-2):53-59.
9. Leveille SG, Ling S, Hochberg MC, et al. Widespread musculoskeletal pain and the progression of disability in older disabled women. *Ann Intern Med.* 2001;135(12):1038-1046.
10. Rudy TE, Weiner DK, Lieber SJ, Slaboda J, Boston JR. The impact of chronic low back pain on older adults: a comparative study of patients and controls. *Pain.* 2007;131(3):293-301.
11. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol.* 1994;49(2):M85-94.
12. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value

of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci.* 2000;55(4):M221-231.
13. Wennie Huang WN, Perera S, VanSwearingen J, Studenski S. Performance measures predict onset of activity of daily living difficulty in community-dwelling older adults. *J Am Geriatr Soc.* 2010;58(5):844-852.
14. Perera S, Patel KV, Rosano C, et al. Gait Speed Predicts Incident Disability: A Pooled Analysis. *J Gerontol A Biol Sci Med Sci.* 2016;71(1):63-71.
15. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA.* 2011;305(1):50-58.
16. Al-Zahrani KS, Bakheit AM. A study of the gait characteristics of patients with chronic osteoarthritis of the knee. *Disabil Rehabil.* 2002;24(5):275-280.
17. Hicks GE, Simonsick EM, Harris TB, et al. Trunk muscle composition as a predictor of reduced functional capacity in the health, aging and body composition study: the moderating role of back pain. *J Gerontol A Biol Sci Med Sci.* 2005;60(11):1420-1424.
18. Sowers M, Jannausch ML, Gross M, et al. Performance-based physical functioning in African-American and Caucasian women at midlife: considering body composition, quadriceps strength, and knee osteoarthritis. *Am J Epidemiol.* 2006;163(10):950-958.
19. White DK, Niu J, Zhang Y. Is symptomatic knee osteoarthritis a risk factor for a trajectory of fast decline in gait speed? Results from a longitudinal cohort study. *Arthritis Care Res (Hoboken).* 2013;65(2):187-194.
20. Coyle PC, Sions JM, Velasco T, Hicks GE. Older Adults with Chronic Low Back Pain: A Clinical Population Vulnerable to Frailty? *J Frailty Aging.* 2015;4(4):188-190.
21. Vlaeyen JW, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. *Pain.* 2000;85(3):317-332.
22. Verbunt JA, Seelen HA, Vlaeyen JW, van der Heijden GJ, Knottnerus JA. Fear of injury and physical deconditioning in patients with chronic low back pain. *Arch Phys Med Rehabil.* 2003;84(8):1227-1232.
23. Cress ME, Meyer M. Maximal voluntary and functional performance levels needed for independence in adults aged 65 to 97 years. *Phys Ther.* 2003;83(1):37-48.
24. Morey MC, Pieper CF, Cornoni-Huntley J. Is there a threshold between peak oxygen uptake and self-reported physical functioning in older adults? *Med Sci Sports Exerc.* 1998;30(8):1223-1229.
25. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med.* 2002;346(11):793-801.
26. Blair SN, Kohl HW, Paffenbarger RS, Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality. A prospective study of healthy men and women. *JAMA.* 1989;262(17):2395-2401.

27. Schrack JA, Simonsick EM, Ferrucci L. The energetic pathway to mobility loss: an emerging new framework for longitudinal studies on aging. *J Am Geriatr Soc.* 2010;58 Suppl 2:S329-336.
28. Schrack JA, Simonsick EM, Chaves PH, Ferrucci L. The role of energetic cost in the age-related slowing of gait speed. *J Am Geriatr Soc.* 2012;60(10):1811-1816.
29. Schrack JA, Simonsick EM, Ferrucci L. The relationship of the energetic cost of slow walking and peak energy expenditure to gait speed in mid-to-late life. *Am J Phys Med Rehabil.* 2013;92(1):28-35.
30. RALSTON HJ. Energy-speed relation and optimal speed during level walking. *Int Z Angew Physiol.* 1958;17(4):277-283.
31. Fleg JL, Morrell CH, Bos AG, et al. Accelerated longitudinal decline of aerobic capacity in healthy older adults. *Circulation.* 2005;112(5):674-682.
32. Shephard RJ. Maximal oxygen intake and independence in old age. *Br J Sports Med.* 2009;43(5):342-346.
33. Fleg JL, O'Connor F, Gerstenblith G, et al. Impact of age on the cardiovascular response to dynamic upright exercise in healthy men and women. *J Appl Physiol (1985).* 1995;78(3):890-900.
34. Martin PE, Rothstein DE, Larish DD. Effects of age and physical activity status on the speed-aerobic demand relationship of walking. *J Appl Physiol (1985).* 1992;73(1):200-206.
35. Hawkins S, Wiswell R. Rate and mechanism of maximal oxygen consumption decline with aging: implications for exercise training. *Sports Med.* 2003;33(12):877-888.
36. Knaggs JD, Larkin KA, Manini TM. Metabolic cost of daily activities and effect of mobility impairment in older adults. *J Am Geriatr Soc.* 2011;59(11):2118-2123.
37. Schols AM, Fredrix EW, Soeters PB, Westerterp KR, Wouters EF. Resting energy expenditure in patients with chronic obstructive pulmonary disease. *Am J Clin Nutr.* 1991;54(6):983-987.
38. Riley M, Elborn JS, McKane WR, Bell N, Stanford CF, Nicholls DP. Resting energy expenditure in chronic cardiac failure. *Clin Sci (Lond).* 1991;80(6):633-639.
39. Wert DM, Brach J, Perera S, VanSwearingen JM. Gait biomechanics, spatial and temporal characteristics, and the energy cost of walking in older adults with impaired mobility. *Phys Ther.* 2010;90(7):977-985.
40. Kang HG, Dingwell JB. Separating the effects of age and walking speed on gait variability. *Gait Posture.* 2008;27(4):572-577.
41. O'Connor SM, Xu HZ, Kuo AD. Energetic cost of walking with increased step variability. *Gait Posture.* 2012;36(1):102-107.
42. Carter CS, Sonntag WE, Onder G, Pahor M. Physical performance and longevity in aged rats. *J Gerontol A Biol Sci Med Sci.* 2002;57(5):B193-197.

43. Ferrucci L, Schrack JA, Knuth ND, Simonsick EM. Aging and the energetic cost of life. *J Am Geriatr Soc.* 2012;60(9):1768-1769.
44. Priede IG. Natural selection for energetic efficiency and the relationship between activity level and mortality. *Nature.* 1977;267(5612):610-611.
45. Wax TM, Goodrick CL. Nearness to death and wheelrunning behavior in mice. *Exp Gerontol.* 1978;13(3-4):233-236.
46. Schrack JA, Zipunnikov V, Simonsick EM, Studenski S, Ferrucci L. Rising Energetic Cost of Walking Predicts Gait Speed Decline With Aging. *J Gerontol A Biol Sci Med Sci.* 2016.
47. Lumley MA, Cohen JL, Borszcz GS, et al. Pain and emotion: a biopsychosocial review of recent research. *J Clin Psychol.* 2011;67(9):942-968.
48. World Health Organization. Health Topics: Physical Activity. 2016; http://www.who.int/topics/physical_activity/en/. Accessed June 23, 2016.
49. Kohl HW, Craig CL, Lambert EV, et al. The pandemic of physical inactivity: global action for public health. *Lancet.* 2012;380(9838):294-305.
50. Holland-Fischer P, Greisen J, Grøfte T, Jensen TS, Hansen PO, Vilstrup H. Increased energy expenditure and glucose oxidation during acute nontraumatic skin pain in humans. *Eur J Anaesthesiol.* 2009;26(4):311-317.
51. Ko SU, Simonsick EM, Ferrucci L. Gait energetic efficiency in older adults with and without knee pain: results from the Baltimore Longitudinal Study of Aging. *Age (Dordr).* 2015;37(1):9754.
52. Gardner AW, Ritti-Dias RM, Stoner JA, Montgomery PS, Scott KJ, Blevins SM. Walking economy before and after the onset of claudication pain in patients with peripheral arterial disease. *J Vasc Surg.* 2010;51(3):628-633.
53. Gussoni M, Margonato V, Ventura R, Veicsteinas A. Energy cost of walking with hip joint impairment. *Phys Ther.* 1990;70(5):295-301.
54. Malatesta D, Simar D, Dauvilliers Y, et al. Energy cost of walking and gait instability in healthy 65- and 80-yr-olds. *J Appl Physiol (1985).* 2003;95(6):2248-2256.
55. Ghamkhar L, Kahlaee AH. Trunk muscles activation pattern during walking in subjects with and without chronic low back pain: a systematic review. *PM R.* 2015;7(5):519-526.
56. Griffin DW, Harmon DC, Kennedy NM. Do patients with chronic low back pain have an altered level and/or pattern of physical activity compared to healthy individuals? A systematic review of the literature. *Physiotherapy.* 2012;98(1):13-23.
57. Stubbs B, Binnekade TT, Soundy A, Schofield P, Huijnen IP, Eggermont LH. Are older adults with chronic musculoskeletal pain less active than older adults without pain? A systematic review and meta-analysis. *Pain Med.* 2013;14(9):1316-1331.
58. Larsson C, Ekvall Hansson E, Sundquist K, Jakobsson U. Impact of pain characteristics and fear-avoidance beliefs on physical activity levels among

older adults with chronic pain: a population-based, longitudinal study. *BMC Geriatr.* 2016;16:50.
59. Maltais DB, Pierrynowski MR, Galea VA, Bar-Or O. Physical activity level is associated with the O2 cost of walking in cerebral palsy. *Med Sci Sports Exerc.* 2005;37(3):347-353.
60. Reisman DS, Rudolph KS, Farquhar WB. Influence of speed on walking economy poststroke. *Neurorehabil Neural Repair.* 2009;23(6):529-534.
61. Roos MA, Rudolph KS, Reisman DS. The structure of walking activity in people after stroke compared with older adults without disability: a cross-sectional study. *Phys Ther.* 2012;92(9):1141-1147.
62. Danks KA, Pohlig RT, Roos MA, Wright TR, Reisman D. The relationship between walking capacity, biopsychosocial factors, self-efficacy and walking activity in individuals post stroke. *Journal of Neurologic Physical Therapy.* 2016.
63. Berthouze SE, Minaire PM, Castells J, Busso T, Vico L, Lacour JR. Relationship between mean habitual daily energy expenditure and maximal oxygen uptake. *Med Sci Sports Exerc.* 1995;27(8):1170-1179.
64. Talbot LA, Metter EJ, Fleg JL. Leisure-time physical activities and their relationship to cardiorespiratory fitness in healthy men and women 18-95 years old. *Med Sci Sports Exerc.* 2000;32(2):417-425.
65. Smeets RJ, Wittink H, Hidding A, Knottnerus JA. Do patients with chronic low back pain have a lower level of aerobic fitness than healthy controls?: are pain, disability, fear of injury, working status, or level of leisure time activity associated with the difference in aerobic fitness level? *Spine (Phila Pa 1976).* 2006;31(1):90-97; discussion 98.
66. Smeets RJ, van Geel KD, Verbunt JA. Is the fear avoidance model associated with the reduced level of aerobic fitness in patients with chronic low back pain? *Arch Phys Med Rehabil.* 2009;90(1):109-117.
67. Convertino VA. Cardiovascular consequences of bed rest: effect on maximal oxygen uptake. *Med Sci Sports Exerc.* 1997;29(2):191-196.
68. Neufer PD. The effect of detraining and reduced training on the physiological adaptations to aerobic exercise training. *Sports Med.* 1989;8(5):302-320.
69. Ferrucci L, Cooper R, Shardell M, Simonsick EM, Schrack JA, Kuh D. Age-Related Change in Mobility: Perspectives From Life Course Epidemiology and Geroscience. *J Gerontol A Biol Sci Med Sci.* 2016;71(9):1184-1194.
70. Simonsick EM, Fan E, Fleg JL. Estimating cardiorespiratory fitness in well-functioning older adults: treadmill validation of the long distance corridor walk. *J Am Geriatr Soc.* 2006;54(1):127-132.
71. Mizner RL, Petterson SC, Clements KE, Zeni JA, Irrgang JJ, Snyder-Mackler L. Measuring functional improvement after total knee arthroplasty requires both performance-based and patient-report assessments: a longitudinal analysis of outcomes. *J Arthroplasty.* 2011;26(5):728-737.

72. Stevens-Lapsley JE, Schenkman ML, Dayton MR. Comparison of self-reported knee injury and osteoarthritis outcome score to performance measures in patients after total knee arthroplasty. *PM R.* 2011;3(6):541-549; quiz 549.
73. Bade MJ, Kohrt WM, Stevens-Lapsley JE. Outcomes before and after total knee arthroplasty compared to healthy adults. *J Orthop Sports Phys Ther.* 2010;40(9):559-567.
74. Brach JS, Vanswearingen JM. Interventions to Improve Walking in Older Adults. *Curr Transl Geriatr Exp Gerontol Rep.* 2013;2(4).
75. Brach JS, Lowry K, Perera S, et al. Improving motor control in walking: a randomized clinical trial in older adults with subclinical walking difficulty. *Arch Phys Med Rehabil.* 2015;96(3):388-394.
76. Delitto A, George SZ, Van Dillen LR, et al. Low back pain. *J Orthop Sports Phys Ther.* 2012;42(4):A1-57.
77. Krein SL, Kadri R, Hughes M, et al. Pedometer-based internet-mediated intervention for adults with chronic low back pain: randomized controlled trial. *J Med Internet Res.* 2013;15(8):e181.
78. McDonough SM, Tully MA, Boyd A, et al. Pedometer-driven walking for chronic low back pain: a feasibility randomized controlled trial. *Clin J Pain.* 2013;29(11):972-981.
79. Roddy E, Zhang W, Doherty M. Aerobic walking or strengthening exercise for osteoarthritis of the knee? A systematic review. *Ann Rheum Dis.* 2005;64(4):544-548.
80. Danks KA, Roos MA, McCoy D, Reisman DS. A step activity monitoring program improves real world walking activity post stroke. *Disabil Rehabil.* 2014;36(26):2233-2236.
81. Danks KA, Pohlig R, Reisman DS. Combining Fast-Walking Training and a Step Activity Monitoring Program to Improve Daily Walking Activity After Stroke: A Preliminary Study. *Arch Phys Med Rehabil.* 2016;97(9 Suppl):S185-193.
82. Fayaz A, Croft P, Langford RM, Donaldson LJ, Jones GT. Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. *BMJ Open.* 2016;6(6):e010364.
83. Leadley RM, Armstrong N, Reid KJ, Allen A, Misso KV, Kleijnen J. Healthy aging in relation to chronic pain and quality of life in Europe. *Pain Pract.* 2014;14(6):547-558.
84. Dominick KL, Ahern FM, Gold CH, Heller DA. Health-related quality of life among older adults with arthritis. *Health Qual Life Outcomes.* 2004;2:5.
85. Lurie J, Tomkins-Lane C. Management of lumbar spinal stenosis. *BMJ.* 2016;352:h6234.
86. Imms FJ, Edholm OG. Studies of gait and mobility in the elderly. *Age Ageing.* 1981;10(3):147-156.

87. Shumway-Cook A, Guralnik JM, Phillips CL, et al. Age-associated declines in complex walking task performance: the Walking InCHIANTI toolkit. *J Am Geriatr Soc.* 2007;55(1):58-65.
88. Larish DD, Martin PE, Mungiole M. Characteristic patterns of gait in the healthy old. *Ann N Y Acad Sci.* 1988;515:18-32.
89. Coyle PC, Schrack JA, Hicks GE. Pain-Energy Model of Mobility Limitation in the Older Adult. *Pain Medicine.* 2017;(in press).
90. Schulte TL, Schubert T, Winter C, et al. Step activity monitoring in lumbar stenosis patients undergoing decompressive surgery. *Eur Spine J.* 2010;19(11):1855-1864.
91. Winter CC, Brandes M, Müller C, et al. Walking ability during daily life in patients with osteoarthritis of the knee or the hip and lumbar spinal stenosis: a cross sectional study. *BMC Musculoskelet Disord.* 2010;11:233.
92. Norden J, Smuck M, Sinha A, Hu R, Tomkins-Lane C. Objective measurement of free-living physical activity (performance) in lumbar spinal stenosis: are physical activity guidelines being met? *Spine J.* 2017;17(1):26-33.
93. Tomkins-Lane CC, Holz SC, Yamakawa KS, et al. Predictors of walking performance and walking capacity in people with lumbar spinal stenosis, low back pain, and asymptomatic controls. *Arch Phys Med Rehabil.* 2012;93(4):647-653.
94. Wood RY, Giuliano KK, Bignell CU, Pritham WW. Assessing cognitive ability in research: use of MMSE with minority populations and elderly adults with low education levels. *J Gerontol Nurs.* 2006;32(4):45-54.
95. Hicks GE, Manal TJ. Psychometric properties of commonly used low back disability questionnaires: are they useful for older adults with low back pain? *Pain Med.* 2009;10(1):85-94.
96. Taylor LJ, Harris J, Epps CD, Herr K. Psychometric evaluation of selected pain intensity scales for use with cognitively impaired and cognitively intact older adults. *Rehabil Nurs.* 2005;30(2):55-61.
97. Borg G. Psychophysical scaling with applications in physical work and the perception of exertion. *Scand J Work Environ Health.* 1990;16 Suppl 1:55-58.
98. Ramos-Jiménez A, Hernández-Torres RP, Torres-Durán PV, et al. The Respiratory Exchange Ratio is Associated with Fitness Indicators Both in Trained and Untrained Men: A Possible Application for People with Reduced Exercise Tolerance. *Clin Med Circ Respirat Pulm Med.* 2008;2:1-9.
99. Papadakis NC, Christakis DG, Tzagarakis GN, et al. Gait variability measurements in lumbar spinal stenosis patients: part B. Preoperative versus postoperative gait variability. *Physiol Meas.* 2009;30(11):1187-1195.
100. Suda Y, Saitou M, Shibasaki K, Yamazaki N, Chiba K, Toyama Y. Gait analysis of patients with neurogenic intermittent claudication. *Spine (Phila Pa 1976).* 2002;27(22):2509-2513.
101. SAUNDERS JB, INMAN VT, EBERHART HD. The major determinants in normal and pathological gait. *J Bone Joint Surg Am.* 1953;35-A(3):543-558.

102. Gardner AW, Montgomery PS, Ritti-Dias RM, Forrester L. The effect of claudication pain on temporal and spatial gait measures during self-paced ambulation. *Vasc Med.* 2010;15(1):21-26.
103. Myers SA, Pipinos II, Johanning JM, Stergiou N. Gait variability of patients with intermittent claudication is similar before and after the onset of claudication pain. *Clin Biomech (Bristol, Avon).* 2011;26(7):729-734.
104. Ladenvall P, Persson CU, Mandalenakis Z, et al. Low aerobic capacity in middle-aged men associated with increased mortality rates during 45 years of follow-up. *Eur J Prev Cardiol.* 2016;23(14):1557-1564.
105. Cleland JA, Whitman JM, Houser JL, Wainner RS, Childs JD. Psychometric properties of selected tests in patients with lumbar spinal stenosis. *Spine J.* 2012;12(10):921-931.
106. Laroche DP, Marques NR, Shumila HN, Logan CR, Laurent RS, Gonçalves M. Excess body weight and gait influence energy cost of walking in older adults. *Med Sci Sports Exerc.* 2015;47(5):1017-1025.
107. Petrovic M, Deschamps K, Verschueren S, et al. Is the metabolic cost of walking higher in people with diabetes? *Journal of Applied Physiology.* 2016;120(1):55-62.
108. Nagai K, Aoyama T, Yamada M, et al. Quantification of changes in gait characteristics associated with intermittent claudication in patients with lumbar spinal stenosis. *J Spinal Disord Tech.* 2014;27(4):E136-142.
109. Lee CE, Simmonds MJ, Etnyre BR, Morris GS. Influence of pain distribution on gait characteristics in patients with low back pain: part 1: vertical ground reaction force. *Spine (Phila Pa 1976).* 2007;32(12):1329-1336.
110. Battié MC, Jones CA, Schopflocher DP, Hu RW. Health-related quality of life and comorbidities associated with lumbar spinal stenosis. *Spine J.* 2012;12(3):189-195.
111. Kalichman L, Cole R, Kim DH, et al. Spinal stenosis prevalence and association with symptoms: the Framingham Study. *Spine J.* 2009;9(7):545-550.
112. Orendurff MS, Schoen JA, Bernatz GC, Segal AD, Klute GK. How humans walk: bout duration, steps per bout, and rest duration. *J Rehabil Res Dev.* 2008;45(7):1077-1089.
113. Cavanaugh JT, Coleman KL, Gaines JM, Laing L, Morey MC. Using step activity monitoring to characterize ambulatory activity in community-dwelling older adults. *J Am Geriatr Soc.* 2007;55(1):120-124.
114. Dunstan DW, Barr EL, Healy GN, et al. Television viewing time and mortality: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab). *Circulation.* 2010;121(3):384-391.
115. Dunstan DW, Howard B, Healy GN, Owen N. Too much sitting--a health hazard. *Diabetes Res Clin Pract.* 2012;97(3):368-376.

116. Healy GN, Dunstan DW, Salmon J, Shaw JE, Zimmet PZ, Owen N. Television time and continuous metabolic risk in physically active adults. *Med Sci Sports Exerc.* 2008;40(4):639-645.
117. Owen N, Healy GN, Matthews CE, Dunstan DW. Too much sitting: the population health science of sedentary behavior. *Exerc Sport Sci Rev.* 2010;38(3):105-113.
118. Stamatakis E, Hamer M, Dunstan DW. Screen-based entertainment time, all-cause mortality, and cardiovascular events: population-based study with ongoing mortality and hospital events follow-up. *J Am Coll Cardiol.* 2011;57(3):292-299.
119. van der Ploeg HP, Chey T, Korda RJ, Banks E, Bauman A. Sitting time and all-cause mortality risk in 222 497 Australian adults. *Arch Intern Med.* 2012;172(6):494-500.
120. Mudge S, Taylor D, Chang O, Wong R. Test-retest reliability of the StepWatch Activity Monitor outputs in healthy adults. *J Phys Act Health.* 2010;7(5):671-676.
121. Bergman RJ, Bassett DR, Muthukrishnan S, Klein DA. Validity of 2 devices for measuring steps taken by older adults in assisted-living facilities. *J Phys Act Health.* 2008;5 Suppl 1:S166-175.
122. Storti KL, Pettee KK, Brach JS, Talkowski JB, Richardson CR, Kriska AM. Gait speed and step-count monitor accuracy in community-dwelling older adults. *Med Sci Sports Exerc.* 2008;40(1):59-64.
123. White DK, Neogi T, Zhang Y, et al. The association of obesity with walking independent of knee pain: the multicenter osteoarthritis study. *J Obes.* 2012;2012:261974.
124. Song J, Semanik P, Sharma L, et al. Assessing physical activity in persons with knee osteoarthritis using accelerometers: data from the osteoarthritis initiative. *Arthritis Care Res (Hoboken).* 2010;62(12):1724-1732.
125. Trost SG, McIver KL, Pate RR. Conducting accelerometer-based activity assessments in field-based research. *Med Sci Sports Exerc.* 2005;37(11 Suppl):S531-543.
126. Jerome GJ, Ko SU, Kauffman D, Studenski SA, Ferrucci L, Simonsick EM. Gait characteristics associated with walking speed decline in older adults: results from the Baltimore Longitudinal Study of Aging. *Arch Gerontol Geriatr.* 2015;60(2):239-243.
127. Sun F, Norman IJ, While AE. Physical activity in older people: a systematic review. *BMC Public Health.* 2013;13:449.
128. Boyle PA, Buchman AS, Wilson RS, Bienias JL, Bennett DA. Physical activity is associated with incident disability in community-based older persons. *J Am Geriatr Soc.* 2007;55(2):195-201.
129. Berk DR, Hubert HB, Fries JF. Associations of changes in exercise level with subsequent disability among seniors: a 16-year longitudinal study. *J Gerontol A Biol Sci Med Sci.* 2006;61(1):97-102.

130. Brach JS, VanSwearingen JM, FitzGerald SJ, Storti KL, Kriska AM. The relationship among physical activity, obesity, and physical function in community-dwelling older women. *Prev Med.* 2004;39(1):74-80.
131. Koho P, Orenius T, Kautiainen H, Haanpää M, Pohjolainen T, Hurri H. Association of fear of movement and leisure-time physical activity among patients with chronic pain. *J Rehabil Med.* 2011;43(9):794-799.
132. Elfving B, Andersson T, Grooten WJ. Low levels of physical activity in back pain patients are associated with high levels of fear-avoidance beliefs and pain catastrophizing. *Physiother Res Int.* 2007;12(1):14-24.
133. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods.* 2007;39(2):175-191.
134. Ellenrieder M, Bader R, Bergschmidt P, Fröhlich S, Mittelmeier W. Coexistent lumbar spine disorders have a crucial impact on the clinical outcome after total hip replacement. *J Orthop Sci.* 2015;20(6):1046-1052.
135. Ben-Galim P, Ben-Galim T, Rand N, et al. Hip-spine syndrome: the effect of total hip replacement surgery on low back pain in severe osteoarthritis of the hip. *Spine (Phila Pa 1976).* 2007;32(19):2099-2102.
136. Bohl WR, Steffee AD. Lumbar spinal stenosis. A cause of continued pain and disability in patients after total hip arthroplasty. *Spine (Phila Pa 1976).* 1979;4(2):168-173.
137. French H, O'Donnell B, Cuddy V, O'Connel P. Clinical features of low back pain in people with hip osteoarthritis: a cross sectional study. *Physiotherapy Practice and Research.* 2015;36:15-22.
138. Stupar M, Côté P, French MR, Hawker GA. The association between low back pain and osteoarthritis of the hip and knee: a population-based cohort study. *J Manipulative Physiol Ther.* 2010;33(5):349-354.
139. Salaffi F, Carotti M, Stancati A, Grassi W. Health-related quality of life in older adults with symptomatic hip and knee osteoarthritis: a comparison with matched healthy controls. *Aging Clin Exp Res.* 2005;17(4):255-263.
140. Hirata S, Ono R, Yamada M, et al. Ambulatory physical activity, disease severity, and employment status in adult women with osteoarthritis of the hip. *J Rheumatol.* 2006;33(5):939-945.
141. Constantinou M, Barrett R, Brown M, Mills P. Spatial-temporal gait characteristics in individuals with hip osteoarthritis: a systematic literature review and meta-analysis. *J Orthop Sports Phys Ther.* 2014;44(4):291-B297.
142. Stone JL, Norris AH. Activities and attitudes of participants in the Baltimore longitudinal study. *J Gerontol.* 1966;21(4):575-580.

Appendix A

IRB APPROVAL LETTER: ENERGY AND PHYSICAL ACTIVITY IN OLDER ADULTS WITH CHRONIC LOW BACK AND RADICULAR LEG PAIN

UNIVERSITY OF DELAWARE
RESEARCH OFFICE

210 Hullihen Hall
University of Delaware
Newark, Delaware 19716-1551
PA: 302/831-2136
Fax: 302/831-2828

DATE: December 23, 2015

TO: Peter Coyle, BS, DPT
FROM: University of Delaware IRB

STUDY TITLE: [841499-1] Energy and Physical Activity in Older Adults with Chronic Low Back and Radicular Leg Pain

SUBMISSION TYPE: New Project

ACTION: APPROVED
APPROVAL DATE: December 23, 2015
EXPIRATION DATE: December 15, 2016
REVIEW TYPE: Full Committee Review

Thank you for your submission of New Project materials for this research study. The University of Delaware IRB has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Full Committee Review based on the applicable federal regulation.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Please note that all research records must be retained for a minimum of three years.

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.

Appendix B

INFORMED CONSENT: ENERGY AND PHYSICAL ACTIVITY IN OLDER ADULTS WITH CHRONIC LOW BACK AND RADICULAR LEG PAIN

INFORMED CONSENT TO PARTICIPATE IN RESEARCH

Title of Project: Energetics & physical activity in older adults with low back and radicular leg pain

Principal Investigator(s): Peter Coyle, PT, DPT
You are being invited to participate in a research study conducted by the Delaware Spine Studies at the University of Delaware. This consent form tells you about the study including its purpose, what you will be asked to do if you decide to take part, and the risks and benefits of being in the study. Please read the information below and ask us any questions you may have before you decide whether or not you want to participate.

WHAT IS THE PURPOSE OF THIS STUDY?
The purpose of this study is to learn more about the energy expenditure and physical activity levels of older adults who have chronic low back pain with leg pain that radiates from their low back. This study will help us understand how painful conditions, like chronic low back pain, may influence the energy expenditure levels and physical activity patterns, for older adults with chronic low back and related leg pain. You will be asked to participate in 2 evaluation sessions at the University of Delaware Clinical Research Laboratory. You will be one of approximately 52 individuals in this study. This study is being conducted as part of a doctoral dissertation. The specific aims of this study are to investigate whether the presence of chronic low back pain with related leg pain impacts the energy required to walk under different walking conditions, as well as daily physical activity patterns.

WHY ARE YOU BEING ASKED TO PARTICIPATE?
You are being asked to participate in our group **with pain** because…

- You are 50-85 years old.
- You have moderately intense chronic (≥3 months duration) low back pain and leg pain that is related to your back.
- Your low back pain radiates to your legs with walking.

- Your low back pain is present on ≥4 days per week.
- You are community-dwelling.

You will not be able to participate in our group **with pain** if:

- You do not pass our mental screening test
- You have difficulty with your hearing or vision that severely restricts your everyday activities.
- You are not English speaking and reading.
- You have any disorders of your brain, spinal cord, or nervous system, including a history of stroke.
- You have high blood pressure that is not controlled by medication, or you have had a heart attack in the past.
- You have been diagnosed with chronic obstructive pulmonary disease (COPD) or peripheral vascular disease.
- You have any areas of pain worse than your low back pain.
- You are unable to walk independently without an assistive device of any kind.

You are being asked to participate in our group **without pain** because…

- You are 50-85 years old.
- You are community-dwelling.

You will not be able to participate in our group **without pain** if:

- You have difficulty with your hearing or vision that severely restricts your everyday activities.
- You are not English speaking and reading.
- You have any disorders of your brain, spinal cord, or nervous system, including a history of stroke.
- You have high blood pressure that is not controlled by medication, or you have had a heart attack in the past.
- You have been diagnosed with chronic obstructive pulmonary disease (COPD) or peripheral vascular disease.
- You have had low back pain within the last year.
- You currently have any areas of significant bodily pain.
- You are unable to walk independently without an assistive device of any kind.

WHAT WILL YOU BE ASKED TO DO?

If you choose to participate, you will be asked to make 2 visits to the Health Sciences complex on the University of Delaware STAR Campus. The first visit will be 1 hour and 40 minutes long, whereas the second will take 30 minutes, for a total of 2 hours

and 10 minutes. In between, you will be asked to wear a step-activity monitor for 7 days, which will be secured to your ankle. As part of this study, you will be asked to complete several questionnaires regarding your physical and psychological health. During the first visit, we will use a lightweight, portable machine connected by a tube to a facemask to measure the amount of oxygen you consume while you rest and during walking over ground. First, we will ask to walk, as your symptoms allow, for up to 20 minutes. Then, after 15 minutes of rest, we will ask you to walk at your maximal speed for 400 meters (i.e. 1/4 mile). In addition to these measures, we will measure your vital signs, height, weight, and different aspects of how you walk on an electronic mat. During the second visit, we will use a stationary machine to measure your oxygen uptake during walking on a treadmill at your usual, comfortable speed for up to 20 minutes or until you no longer wish to walk. Prior to each visit, you will be asked to not consume caffeine or exercise for 12 hours before your evaluation, and to avoid eating for 3 hours prior to your visit. However, you may take your prescribed medication, and we encourage you to drink plenty of water. A small snack (i.e. granola bar) will be provided at the end of each session. For seven days in between sessions, you will be asked to wear a small, lightweight device around your ankle, which will measure the amount of physical activity you perform.

Complete questionnaires that will be mailed to you prior to coming to your **first** visit

Visit 1

- First Visit (1 hour 40 minutes) located in the Clinical Research Laboratory
  - Informed consent (10 minutes)
  - Evaluation for Eligibility (5 minutes)
  - Vital Signs (10 minutes)
  - Gait analysis (10 minutes)
  - Over Ground Submaximal Walking Test (15 minutes)
  - Rest Break (15 minutes)
  - Over Ground Maximal Walking Testing (25 minutes)
  - Step Monitor set up and education on use (10 minutes)

At Home

- At home
  - Wear the Step Monitor and complete daily activity logs for 7 days
  - Return the monitor and logs in self-addressed, pre-stamped envelope, or bring to second visit

Visit 2

- Second Visit (30 minutes) located in the Clinical Research Laboratory
  - Treadmill Submaximal Walking Test (30 minutes)
- Compensation $40

Questionnaires (about 30 minutes in length):
We will ask you to complete questionnaires related to your age, marital status, race/ethnicity, education level, medical history and current medications. We will also ask you to complete questionnaires related to your low back pain, physical activity level, fatigue, sleep patterns, and mood. Completion of all questionnaires is completely voluntary.

Eligibility Screening (about 5 minutes in length):
We will ask you some questions to determine if you are eligible to participate in this study. If you meet the criteria, you will be cleared for full participation. If you do not meet the criteria, you will not be able to participate in this study and we will destroy your data.

Vital Signs & Anthropometrics (about 10 minutes in length):
We will assess your resting vital signs, including blood pressure in each arm, heart rate, and respiratory rate. We will collect your height and weight, to calculate body mass index. We will also measure your waist and hip size, using a flexible tape measure.

Walking Analysis (about 10 minutes in length):
We will have you walk across an electronic walkway at different speeds. The walkway will collect information about your walking speed, your step length, and your base of support, among other things.

Over Ground Sub-maximal Walk Test (about 25 minutes in length):
After fasting from food (3 hours prior to visit) and caffeine (12 hours prior to visit), we will measure the amount of oxygen you consume during different conditions. We will place a facemask on you, which covers your nose/mouth and secures to your head. Headgear consisting of Velcro straps will be used to keep the mask around your mouth and nose. This mask will ensure a seal around the mouth, so that we may accurately collect the amount of oxygen and carbon dioxide that you exhale. This mask will be connected to a tube, which will, in turn, connect to a compact, portable machine that analyzes the gas. We will ask you to wear this light-weight device in a chest harness specifically designed for this test. First, we will ask you to walk for up to 10 minutes, or until you need to stop because of pain or discomfort, around a marked course. For this test, we will ask that you walk at your normal, comfortable pace. Occasionally, we will ask you to rate your how intense your symptoms are and your perceived level of exertion during this test.

Over Ground Maximal Walk Test (about 30 minutes in length):
Next, we will have you sit in a chair for 15 minutes to allow you to recover from the first walking test. We will ask you to walk 400 meters around a marked course, as fast as you possibly can. There will be 20 meters between each cone, so 400 meters will be

10 full laps. This test will be able to allow us to estimate the peak amount of oxygen you inhale and exhale during activity, which is an important marker of fitness. We will ask you to rate your pain intensity before and after completing the test, as well as the amount of exertion the test took on your part. Like other aspects of this study, this is voluntary.

Physical Activity Monitoring (7 days, at home):
You will be asked to wear a StepWatch Activity Monitor, around your ankle, for seven full days after your first visit. This monitor is a lightweight device that secures to your ankle; it will measure how far you walk while wearing the device. In addition, we will ask you to complete an activity log for each day that you wear it. We will ask you to wear the device during all waking hours, but to remove it for sleeping, showering/bathing, and swimming.

Over Ground Sub-maximal Walk Test (about 30 minutes in length):
After following the same fasting instructions as visit 1, we will perform another walking test at visit 2. This test will be performed on the treadmill at your usual, comfortable speed. We will use a device similar to that of the first visit; this device will be stationary, meaning you will not have to wear a chest harness. We will ask you to walk for up to 10 minutes, or until you need to stop because pain or discomfort, on the treadmill at a constant speed. For this test, we will ask that you walk at your normal, comfortable pace. Occasionally, we will ask you to rate your how intense your symptoms are and your perceived level of exertion during this test.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?
There are no known risks with vital signs, height, weight, and body circumference. Possible risks of participating in this research study include a potential, temporary increase in your low back and leg symptoms with walking tests. If you are diabetic, there is a small risk of hypoglycemia with fasting; please, continue to routinely monitor your blood sugar and we will provide you with a snack should you feel that your blood sugar is running low. Additionally, you may experience some discomfort related to the amount of exertion, particularly with walking at your maximal speed. However, we will be monitoring your pain intensity, as well your heart rate during these tests. Although the risk of having a cardiac events is low (approximately 6 in 10,000 stress tests), if you experience chest/neck pain, dizziness, shortness of breath, or nausea, the session will be stopped and your physician will be contacted. We expect this risk to be even lower, since these walking conditions are comparable to real world living, not stress testing, and you do not have any uncontrolled or significant cardiovascular health conditions.

You may choose to stop walking at any point during these tests. An emergency stop button will be within your reach and for your use while you are on the treadmill. We also have scheduled walking testing on two different days to allow your symptoms to

subside, should you have any with testing. There is a risk of falling with these walking tasks, but a licensed physical therapist will be with you during all aspects of the study to minimize this risk.

WHAT IF YOU ARE INJURED DURING YOUR PARTICIPATION IN THE STUDY?

If you are injured during research procedures, you will be offered first aid at no cost to you. If you need additional medical treatment, the cost of this treatment will be your responsibility or that of your third-party payer (for example, your health insurance). By signing this document, you are not waiving any rights that you may have if injury was the result of negligence of the university or its investigators.

WHAT ARE THE POTENTIAL BENEFITS?

A potential benefit of this study is receiving the results of your vital sign and body measurement screen, and the explanation of the normal ranges and health risks associated with your measurements. Although this study only includes three bouts of walking, moderate and vigorous levels physical activity are associated with positive physical and psychological health benefits. Furthermore, the knowledge gained from this study will improve our understanding of *how* low back and related leg pain may cause physical disability. In the future, the results provided from this study will lay the groundwork for interventions aimed at quality of life improvement and disability prevention, in older adults with and without these painful conditions.

NEW INFORMATION THAT COULD AFFECT YOUR PARTICIPATION:

During the course of this study, we may learn new information that could be important to you. This may include information that could cause you to change your mind about participating in the study. We will notify you as soon as possible if any new information becomes available.

HOW WILL CONFIDENTIALITY BE MAINTAINED? WHO MAY KNOW THAT YOU PARTICIPATED IN THIS RESEARCH?

Research records of your evaluation will be maintained in the Clinical Research Laboratory (540 S. College Ave). Files will be secured in locked cabinets. Only research personnel will have access to the data. De-identified data will be entered from the record to a computerized database where all participants will be identified by only a code number. You information will be indefinitely stored using a coded number. Additionally, in a separate database, we will also maintain your name and contact information if you agree to be contacted for future studies. Neither your name nor personal information will be used in any publication or presentation from this study. The confidentiality of your records will be protected to the extent permitted by law. Your research records may be viewed by the University of Delaware Institutional Review Board, which is a committee formally designated to approve, monitor, and review biomedical and behavioral research involving humans.

USE OF DATA COLLECTED FROM YOU IN FUTURE RESEARCH: (Only if applicable)
The research data we will be collecting from you during your participation in this study may be useful in other research studies in the future. Your choice about future use of your data will have no impact on your participation in this research study. Do we have your permission to use in future studies data collected from you? Please write your initials next to your preferred choice.

_____ YES **_____ NO**

WILL THERE BE ANY COSTS TO YOU FOR PARTICIPATING IN THIS RESEARCH?
There are no costs associated with participating in this study.

WILL YOU RECEIVE ANY COMPENSATION FOR PARTICIPATION?
You will be compensated with a $40 Visa gift card for the completion of testing, and we will pro-rate the total for partial participation.

DO YOU HAVE TO TAKE PART IN THIS STUDY?
Taking part in this research study is entirely voluntary. You do not have to participate in this research. If you choose to take part, you have the right to stop at any time. If you decide not to participate or if you decide to stop taking part in the research at a later date, there will be no penalty or loss of benefits to which you are otherwise entitled.

Your decision to stop participation, or not to participate, will not influence current or future relationships with the University of Delaware

WHO SHOULD YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?
If you have any questions about this study, please contact the Principal Investigator, Peter Coyle, at 302-831-7142 or pcoyle@udel.edu. You can also contact Peter's advisor and co-investigator, Gregory Hicks, at 302-831-2690 or ghicks@udel.edu. If you need to contact Peter while wearing the step activity monitor, the 24-hour contact number is 302-831-7142. If he is unable to answer the phone of if it outside of the hours of 8:00am – 5:00pm, please leave a detailed message. This message will be automatically sent to Peter and he will contact you as soon as possible. If you have any questions or concerns about your rights as a research participant, you may contact the University of Delaware Institutional Review Board at hsrb-research@udel.edu or (302) 831-2137.

Your signature on this form means that: 1) you are at least 18 years old; 2) you have read and understand the information given in this form; 3) you have asked

any questions you have about the research and those questions have been answered to your satisfaction; 4) you accept the terms in the form and volunteer to participate in the study. You will be given a copy of this form to keep.

_____	_____
Printed Name of Participant Date	Signature of Participant
_____	_____
Person Obtaining Consent Date	Person Obtaining Consent
(PRINTED NAME)	(SIGNATURE)

<u>OPTIONAL</u> CONSENT TO BE CONTACTED FOR FUTURE STUDIES:

Do we have your permission to contact you regarding participation in future studies? Please write your initials next to your preferred choice.

_____ YES _____ NO

Appendix C

DATA TRANSFER AGREEMENT: BALTIMORE LONGITUDINAL STUDY OF AGING

NATIONAL INSTITUTE ON AGING, INTRAMURAL RESEARCH PROGRAM
LETTER AGREEMENT FOR THE TRANSFER OF DATA

In response to the RECIPIENT's request for the following data and all tangible representations thereof ("DATA"): De-identified patient data from individuals collected under PROVIDER'S IRB-approved protocol #03-AG-0325 entitled, "Longitudinal Studies of Human Physiology, Biochemistry, and Psychology (The Baltimore Longitudinal Study of Aging)", the PROVIDER asks that the RECIPIENT and the RECIPIENT SCIENTIST agree to the following before the RECIPIENT receives the DATA:

1. The above DATA is the property of the PROVIDER and is made available as a service to the research community.

2. THIS DATA WILL NOT BE USED TO TREAT OR DIAGNOSE HUMAN SUBJECTS.

3. The DATA will be used for teaching or not-for-profit research purposes only.

4. The DATA will not be further distributed to others without the PROVIDER's written consent. The RECIPIENT shall refer any request for the DATA to the PROVIDER.

5. The RECIPIENT SCIENTIST agrees to acknowledge the contribution of the PROVIDER in all written or oral public disclosures concerning RECIPIENT's research using the DATA, by acknowledgment or co-authorship at the discretion of the PROVIDER. RECIPIENT agrees to supply the PROVIDER with copies of experimental results obtained from the use of this DATA at least thirty (30) days prior to publication or any other public disclosure.

6. THE PROVIDER MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE DATA WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER PROPRIETARY RIGHTS. Unless prohibited by law, RECIPIENT assumes all liability for claims for damages against it by third parties which may arise from the use, storage or disposal of the DATA except that, to the extent permitted by law, the PROVIDER shall be liable to the RECIPIENT when the damage is caused by the gross negligence or willful misconduct of the PROVIDER.

7. The RECIPIENT agrees to use the DATA in compliance with all applicable statutes and regulations.

8. The DATA is provided at no cost, or with an optional transmittal fee solely to reimburse the PROVIDER for its preparation and distribution costs. If a fee is requested, the amount will be

indicated here: none

9. The DATA has been collected from human subjects. The DATA has been collected under an IRB approved protocol in accordance with federal guidelines for "Protection of Human Subjects."

10. Participant identifying information will not be provided. The DATA may be protected by the Federal Privacy Act and/or a Certificate of Confidentiality. RECIPIENT and RECIPIENT SCIENTIST agree to comply with all applicable statutes, regulations and ethical requirements to protect the identity and privacy of human subjects from whom the DATA was collected.

11. If either party transfers written confidential information concerning the DATA and/or the Research Project (as defined in Article 14) hereinafter, "Confidential Information", then to the extent permitted by law, receiving party agrees to treat in confidence, for a period of three (3) years from the date of its disclosure, any of the providing party's written Confidential Information about this DATA and/or the Research Project that is stamped "CONFIDENTIAL," except for information that: (a) is publicly known, or available from other sources who are not under a confidentiality obligation to the source; (b) has been made available by its owners without a confidentiality obligation; (c) is otherwise already known by or available to the receiving party without a confidentiality obligation; or (d) is required to be disclosed by operation of law, provided that party required to disclose such information takes reasonable and lawful actions to avoid and/or minimize such disclosure. Any oral disclosures from the disclosing party to the receiving party shall be reduced to writing and identified as being CONFIDENTIAL by written notice delivered to the receiving party within thirty (30) days after the date of the oral disclosure.

12. This Agreement is effective for a period of five (5) years from the date of final signature of this Agreement. Either Party may terminate this Agreement with thirty (30) days written notice to the other Party. In the event this Agreement is terminated, RECIPIENT shall promptly return to PROVIDER or, at PROVIDER'S option, destroy all copies of DATA. Upon PROVIDER's request, RECIPIENT shall confirm in writing as to such destruction.

13. When the research is completed, any Confidential Information will be returned to PROVIDER according to the PROVIDER's instructions. However, RECIPIENT may keep one (1) copy of the Confidential Information to document its obligations under this agreement.

14. DATA will be used by RECIPIENT SCIENTIST solely in connection with the following Research Project:

- **Research Project Title: Energetic Inefficiency as Predictor for Decline in Aerobic Capacity among BLSA Volunteers with and without Low Back Pain**

The PROVIDER, RECIPIENT and RECIPIENT SCIENTIST must sign both copies of this letter and return one signed copy to the PROVIDER. The PROVIDER will then send the DATA.

RECIPIENT INFORMATION and AUTHORIZED SIGNATURE

RECIPIENT: University of Delaware
RECIPIENT SCIENTIST: Peter Coyle, PT, DPT
Recipient Address: 540 South College Ave, Suite 144A
Newark, DE 19713

Signature of Authorized Official — Date: 5/18/16

Please address all correspondence related to this agreement to Peter Coyle, PT, DPT at the following address by express mail:
540 South College Ave, Suite 144A, Newark, DE 19713

PROVIDER INFORMATION and AUTHORIZED SIGNATURE

PROVIDER: National Institute on Aging
Provider Scientist: Luigi Ferrucci, MD, PhD
Provider Address: National Institute on Aging, NIH
Address: Harbor Hospital, 5th Floor, 3001 S. Hanover Street, Baltimore, MD 21225

Signature of Authorized Official or designee — Date
Josephine M. Egan, M.D.
Title: Clinical Director
Address: 3001 S. Hanover Street, Baltimore, MD 21225

Stephanie Studenski, M.D., M.P.H. — Date
Title: BLSA Director
Address: 3001 S. Hanover Street, Baltimore, MD 21225

CC: Clinical Director, NIA
NIA Clinical Research Protocol Office