DO INDIVIDUALS WITH KNEE OSTEOARTHRITIS WALK WITH DISTINCT KNEE BIOMECHANICS AND MUSCLE ACTIVATION CHARACTERISTICS? AN INVESTIGATION OF KNEE OSTEOARTHIRITS, HIP OSTEOARTHRITIS, AND ASYMPTOMATIC GROUPS.

by

Jessica D. J. Lohnes

Submitted in partial fulfilment of the requirements
for the degree of Masters of Science

at

Dalhousie University
Halifax, Nova Scotia
December 2021

Table of Contents

List of Tables

List of Figures

Abstract

Knee osteoarthritis is a musculoskeletal condition affecting mobility and function. Hallmark biomechanical indicators have been linked knee OA severity and progression, yet it remains unknown whether these are exclusive to the OA knee. Thesis objectives were to determine whether these gait outcomes were unique to those with knee OA by concurrently investigating groups of asymptomatic individuals and those with hip OA. Forty-eight participants walked on an instrumented treadmill while knee motion, ground reaction forces, and electromyographic signals were collected. Lateral: medial activation ratios were computed for the surrounding knee muscles. Hamstring muscle activation is affected by hip OA in a direction opposite to knee OA and provides a gait outcome that is unique in the knee OA disease. In the other studied features, similarities either exist between hip OA and knee OA (sagittal plane moments), or asymptomatic and knee OA (frontal plane moments) or all three groups (sagittal plane motion).

List of Abbreviations Used

ACR- American College of Rheumatology

ANOVA- Analysis of Variance

BMI – Body Mass Index

COP- Center of Pressure

DOF- Degrees of Freedom

EMG- Electromyography

EULAR - European League Against Rheumatism

GRF- Ground Reaction Forces

HOOS- Hip Osteoarthritis Outcome Score

ICC- Intraclass Correlation Coefficients

ICF- International Classification of Functioning Disability and Health

JAR- Joint Action Research laboratory

KAM- Knee Adduction Moment

KFM- Knee Flexion Moment

KJC- Knee Joint Center

KL- Kellgren Lawrence

LG- Lateral Gastrocnemius

LH- Lateral Hamstrings

MDC- Minimal Detectable Change

MG- Medial Gastrocnemius

MH- Medial Hamstrings

MVIC- Maximum Voluntary Isometric Contraction

NSHA- Nova Scotia Health Authority

NSHRF- Nova Scotia Health Research Foundation

OA- Osteoarthritis

OARSI- Osteoarthritis Research Society International

PCA- Principal Component Analysis

REB- Research Ethics Board

RF- Rectus Femoris

RMS- Root Mean Square

SENIAM- Surface EMG for the Non-Invasive Assessment of Muscles

SD- Standard Deviation

THR- Total Hip Replacement

TKA- Total Knee Arthroplasty

VL- Vastus Lateralis

VM- Vastus Medialis

WHO- World Health Organization

Acknowledgements

There are many people I would like to thank for enriching my experience as a Masters student in the School of Physiotherapy at Dalhousie University. First and foremost, I would like to sincerely thank my supervisor Dr. Derek Rutherford for his continuous support, words of encouragement, and patience throughout this degree. His passion for research is infectious, and his curiosity and dedication are inspiring. He challenges his students to think critically about their projects and how they apply to the clinical setting. He is devoted to narrowing the gap between research and clinical practice, and I cannot express how appreciative I am to have him as a mentor. I will carry the knowledge I gained through his guidance into my career as a physiotherapist.

I would also like to thank Dr. Rebecca Moyer and Dr. Janice Moreside for serving as committee members on this project. Your breadth of knowledge, time commitment, and insightful feedback did not go unnoticed. To everyone I had the privilege of working with at the Joint Action Research Lab, I thank you for sharing your experience and expertise with me as we navigated through our projects. A special thanks to Dr. Matt Baker and Carson Halliwell for creating a fun environment to work in, and the endless laughter we shared.

Finally, I would like to thank my friends and family for their everlasting support. These last few years have been difficult to say the least, and they inspired me to never give up. Finally, a special thanks to my partner Ifedayo Abel-Adegbite for the endless encouragement (and occasional bribe) to keep going. Without any of these people, this thesis would not have been possible.

Chapter 1 - Introduction

1.1 Introduction

Osteoarthritis (OA) is a highly prevalent, multidimensional musculoskeletal condition in adults with significant bearings on the health and quality of life of those affected.[1–3] In Canada, over 4.4 million individuals are living with OA, with this number expected to increase considerably in the following years.[1] The impact of this disease is widespread, creating socioeconomical burdens at the individual, community, and national levels. Individuals with OA are faced with greater financial encumbrances, require more frequent care from health professionals,[4,5] and often have difficulty executing activities of daily living[6] and employment requirements.[7,8] These are closely followed by a national economic burden, as productivity loss due to illness and disability continues to rise[9] and resources for managing OA in Canada's health care system are stretched.[10] There is no current cure of OA despite many management guidelines available.[11–14] It is not entirely clear how these management plans target the multidimensionality of OA or what outcomes we should monitor to determine impact. Without these data, we will struggle to find a way to mitigate the burden of OA in Canada and indeed the world.

While the exact etiology of OA remains unknown, it is generally attributed to a combination of maladaptive biological, mechanical, and structural responses to abnormal mechanical stresses.[15–18] In a healthy joint, physiological loading is necessary to stimulate the biosynthesis of new cells and preserve tissue integrity.[19] This homeostatic environment can be disrupted by excessive joint loading, malalignment of joint structures, or a combination of both,[16] thereby negatively impacting the metabolism of

joint cells leading to an imbalance of anabolic and catabolic activity and resulting in joint degradation.[15,18]

Degradation of lower extremity joints can be highly debilitating, often leading to a decline in functional ability[20,21] and increased risk for comorbidities.[1,22] For many, the capacity to remain physically active lies within their ability to walk, yet many individuals with OA struggle with this task. In fact, symptomatic knee and hip OA was found to be the greatest contributor to walking difficulty in older adults.[22] To better understand the relationships between joint function and limitations in activities such as walking, biomechanical gait analyses have evolved allowing objective evaluations of mechanical demands in healthy and pathological joints during walking.

For over a decade, researchers have demonstrated that individuals with lower extremity OA show characteristic alterations in their joint mechanics during gait. For people with medial compartment knee OA, the most commonly reported metrics include altered sagittal and frontal plane motions,[23–29] as well as joint moments,[23,28,30–34] with the latter providing an understanding of the mechanical demands on the knee joint tissues. In people with hip OA, hip joint mechanics are primarily altered in the sagittal plane, where reduced hip joint extension[35–39] and lower peak hip flexion-extension moments[35,37,39] are commonly identified features during gait. Together, joint mechanics are shown to be different from an asymptomatic group when studying the symptomatic joint in OA, even at early stages of the disease process. If one joint is affected by OA, what happens to the other joints in the lower extremity during walking? The focus of this thesis is on the knee joint of people with moderate knee OA, moderate hip OA, and an asymptomatic group, to

help address this question. Are knee joint biomechanical and neuromuscular alterations associated with knee OA distinct to the disease?

In comparison to asymptomatic individuals, sagittal plane biomechanics are altered where osteoarthritic knees tend to remain in a flexed position at the time of initial contact and move less throughout the loading response and stance phase of the gait cycle.[23–29] Additionally, changes have been reported to occur in the flexion-extension moment with the presence of disease, which is reflective of all agonist and antagonist muscles crossing the knee joint.[40] Individuals with knee OA demonstrate a reduction in the difference between the peak flexion and extension moments, representing a less dynamic sagittal plane loading pattern.[23,28,31–33] The combination of these variations has been referred to as "dynamic joint stiffness" or "stiff gait" and may represent an attempt to improve knee joint stability as the structural integrity of the articulating surfaces are compromised,[31] and has been associated with increasing disease severity.[23,27]

In the frontal plane, the net external knee adduction moment (KAM), has been a biomechanical feature of interest in knee OA gait literature, representing the medial-to-lateral tibiofemoral compartment joint load distribution.[30,34,41] Several studies have reported an increased KAM in individuals with knee OA in comparison to healthy controls,[23,28,30,42] as well as in those of greater severities.[23,34,42] The KAM has also been consistently related to disease progression.[43–45] Several longitudinal studies have shown associations between the KAM and radiographic measures of disease advancement, such as Kellgren Lawrence (KL) grades,[43] medial joint space narrowing,[43] medial cartilage volume,[44] and medial-to-lateral cartilage thickness ratios[45] over periods of one to six years.

Collectively, these studies provide evidence that both sagittal plane and frontal plane mechanics are altered with the presence and progression of knee OA. Reductions in flexion-extension motion and moments suggest a less dynamic, or stiffer, gait pattern in osteoarthritic knees, while increases in the frontal plane KAM represents a loading distribution biased towards the medial knee compartment. These findings are consistently reported in the literature, both of which have been demonstrated in comparison to asymptomatic knees, and with advancing disease severity.

While knee biomechanics have contributed to our understanding of joint function in knee OA, they are limited in providing an understanding of how joint function may be maintained through muscle activation during gait. Electromyography (EMG) studies of knee joint muscles during walking have typically shown individuals with knee OA affecting the medial tibiofemoral compartment preferably activate their lateral knee musculature over the medial.[28,46–52] This seems particularly true for the hamstring muscles, as increased lateral hamstring (LH) activity has been reported in individuals with knee OA in comparison to healthy controls,[28,46,47,50–52] and to medial hamstring (MH) activations.[46,49,53]

The differential activation has been proposed as a protective mechanism to counteract the high medial compartment knee joint loading often present in knee OA.[46] Heiden and colleagues (2009) reported this laterally directed contraction strategy was more pronounced with increasing KAM in individuals with knee OA and was suggested to be a learned motor pattern in attempt to counteract the increasing KAM and associated disease symptoms.[25] Another theory for the heightened LH activity present in individuals with knee OA is that it is a reflexive response to the lateral compartment tensile stresses

experienced as a result of the dynamic varus malalignment typically associated with the presence and progression of medial compartment knee OA.[54–57] This explicit differential activation has not been reported in asymptomatic adults,[46,53] the contralateral knee of knee OA patients,[53,58] nor younger adults or those with hip injuries,[59] and thus may be unique to knee OA pathology and provide information regarding disease progression.

While these biomechanical and neuromuscular adaptations associated with knee OA presence and progression remain rather consistent, little is known about their uniqueness to the disease. In fact, whether they represent pathomechanics distinctive of knee OA exclusively or of a lower-extremity pathology in general remains unknown. Most often, when OA is discussed in the literature, the most symptomatic joint remains the focus. Unfortunately, this picture is incomplete, as epidemiological studies have shown that a significant number of OA patients develop pathologies in at least two of the three lower-extremity weight bearing joints, suggesting problems in one joint may be biomechanically related to problems in others.[60,61]

Using hip OA as a comparator, research pertaining to knee mechanics in individuals with hip OA exists but is limited to date. A study could not be found where a head-to-head comparison of knee mechanics between individuals with moderate knee OA and moderate hip OA has been conducted in relation to an asymptomatic group. Previous hip OA studies have focused on contralateral limb loading via the KAM following total hip joint replacement (THR) procedures.[62–65] Others have studied ipsi- and contra- lateral sagittal plane mechanics, and knee joint muscle activation patterns.[39,66,67] Sagittal plane knee joint motion has shown to be reduced both bilaterally[66] and on the affected limb[39] of individuals with moderate hip OA compared to asymptomatic controls. As the knees of

individuals with hip OA transition from peak flexion to peak extension during mid-to-late stance, they remained in a flexed position and do not move fully into extension, representing a stiffer movement pattern.[39,66] Rutherford and collaborators (2018) reported this reduction in knee joint motion is more pronounced in the ipsilateral than contralateral limbs, and becomes less dynamic with increasing hip OA disease severity.[67] These alterations are parallel to those described in individuals with knee OA, yet the individuals with hip OA showed no symptoms or clinical evidence of knee OA. Why does the ipsilateral knee of individuals with hip OA seem to move like an OA knee? What is it about these features linked to knee OA progression that are in fact true drivers behind structural degradation?

Osteoarthritis is a debilitating disease with significant influences on mobility and function. Using gait analysis techniques, characteristic pathomechanical alterations have been identified in individuals with symptomatic medial compartment knee OA and shown association to progression and severity of the disease. Biomechanical markers such as an increase in KAM, among reductions in sagittal plane motion, moments, and differential muscle activations have been identified as hallmark indicators of knee OA. However, whether these commonly identified features of knee OA gait are unique to the diseased joint or representative of a unilateral lower-extremity pathology in general, remains inconclusive. Individuals with hip OA have also shown similar alterations in knee gait mechanics compared to an asymptomatic population, yet the focus remains on the contralateral knee. How hip OA affects mechanics of the knee on the same side as the pathology, and whether those alterations are equivalent to adaptations identified with knee OA is yet to be determined. Understanding exclusive qualities of knee OA gait that

are present early in the disease process is crucial to continue the evolution of effective management and treatment strategies.

1.2 Overall Objective

To date, there is no clear understanding how knee joint mechanics of individuals with knee OA compare to a group with another lower extremity pathology. Characteristic mechanical and neuromuscular activations coinciding with the presence and progression of knee OA have been consistently identified in the literature, some of which have also been identified to occur in ipsilateral knee of individuals with hip OA. Therefore, the main objective of this thesis was to determine whether specific biomechanical and neuromuscular gait outcomes previously linked to symptomatic medial compartment knee OA severity and progression are in fact unique to those with knee OA by concurrently investigating a group of asymptomatic individuals and those with moderate hip OA, with each comparator group having no known knee OA.

1.3 Specific Objectives

The specific study objectives were:

1. To determine if the sagittal plane movement dynamics (range from peak flexion to peak extension moments, and ranges of motion through loading response and mid-to-late stance) in individuals with symptomatic unilateral medial compartment knee OA are different from the ipsilateral knee of individuals with symptomatic unilateral moderate hip OA, and asymptomatic individuals.
2. To determine if the peak KAM and KAM impulse in individuals with symptomatic unilateral medial compartment knee OA are different from the

ipsilateral knee of individuals with symptomatic unilateral moderate hip OA, and asymptomatic individuals.

3. To determine if the difference in lateral and medial quadriceps, hamstring, and gastrocnemius activation levels in individuals with symptomatic unilateral medial compartment knee OA is different from the ipsilateral knee of individuals with symptomatic unilateral moderate hip OA, and asymptomatic individuals.

1.4 Hypotheses

It was hypothesized:

- The range of sagittal plane moments from peak flexion to peak extension would be reduced in individuals with knee OA in comparison to the hip OA and asymptomatic groups. There would be no differences between hip OA and asymptomatic groups.
- The knee OA group would demonstrate heightened peak KAM and KAM impulse measures in comparison to both the hip OA and asymptomatic groups. There would be no differences between hip OA and asymptomatic groups.
- There would be a higher lateral: medial hamstring (LH:MH) activation ratio in the knee OA group compared to the hip OA and asymptomatic groups. There would be no differences between hip OA and asymptomatic groups, nor any between-group differences for lateral: medial quadriceps (VL:VM) nor lateral: medial gastrocnemius (LG:MG) activation ratios.

Chapter 2 - Review of Relevant Literature

2.1 Introduction to Osteoarthritis

Osteoarthritis is reported as the single most common cause of disability in older adults.[68] More than 4.4 million Canadians are living with OA, with this number expected to exceed ten million over the next 30 years.[1] Osteoarthritis is characterized as a whole joint disease that impacts joint integrity at the anatomic, molecular and physiologic levels.[69] The Osteoarthritis Research Society International (OARSI) defines OA as "a disorder involving movable joints characterized by cell stress and extracellular matrix degradation initiated by micro- and macro-injury that activates maladaptive repair responses including pro-inflammatory pathways of innate immunity. The disease manifests first as a molecular derangement (abnormal joint tissue metabolism) followed by anatomic, and/or physiologic derangements (characterized by cartilage degradation, bone remodeling, osteophyte formation, joint inflammation and loss of normal joint function), that can culminate in illness".[69]

As evidenced in the recent OARSI definition, OA is a heterogeneous condition considerate of both a disease and an illness. The American College of Rheumatology (ACR) criteria for diagnosis of OA is commonly used and considers a combination of clinical features, laboratory test results, and radiographic findings in the diagnosis. This criterion was developed in the 1980's using a control group with over half of the patients diagnosed with rheumatoid arthritis,[70] thus making them more useful for differentiating knee OA from inflammatory arthritis, rather than for diagnosis of knee OA itself.[71] In 2017, the European League Against Rheumatism (EULAR) released evidence-based recommendations on the use of imaging in the management of symptomatic peripheral

joint OA and declared the use of imaging for OA diagnosis is not recommended in cases with typical disease presentation.[12] A confident diagnosis with an estimated probability of up to 99% for the presence of knee OA can be made in the primary care setting without the use of imaging based upon the following six signs and symptoms: persistent knee pain, short-lived morning stiffness, functional limitation, crepitus, restricted movement, and bony enlargement. The more positive results a patient presents with, the more likely the diagnosis of OA.[71] Together these data emphasize the importance of considering the diverse presentations of lower limb OA and to determine appropriate identification and management methods.

There is no cure for OA. Current treatment efforts are often focused on reducing symptoms until late stages of structural progression, when joint replacement is the only option.[64,72,73] As noted, this multidimensional disease is defined as having both a disease and an illness component. Although these terms are often used interchangeably, they are characteristically different.[69] Cassell (1976) describes illness as "what the patient feels when he goes to the doctor" and disease refers to "what he has on the way home from the doctor's office".[74] Disease refers to abnormalities of structure or function in bodily tissues, such as cartilage degeneration, while illness refers to the subjective human response to disease, such as symptoms of pain and stiffness.[75] In OA, it is common for disease and illness components to exist independently, where an individual may have definite structural evidence of OA without the coinciding symptoms or functional deficits or, the other way around,[69] making the identification and management of this complex condition difficult.

The extent to which OA impacts an individual is difficult to truly determine. Not only is the presentation of OA a multidimensional plethora of factors related to illness and disease, potential exists for multiple lower extremity joints to be affected. Indeed, management and scientific inquiry has focused on the most symptomatic joint, yet degeneration in one large joint has been associated with degenerative changes in other large joints.[62,64,76] Epidemiological studies have shown that a significant number of knee OA patients have pathologies in at least two of the three lower extremity weight-bearing joints, suggesting that problems in one joint may be biomechanically related to problems in others.[60,61]

As an example, Metcalfe and associates (2012) reported that 80% of individuals with unilateral knee OA at baseline progressed to having bilateral radiographic changes within 12 years.[77] Furthermore, it has been shown that 34% of women with unilateral knee OA progressed to bilateral knee OA within only two years' time.[78] In fact, many individuals receiving a knee or hip replacement because of advanced unilateral osteoarthritis, will go on to require a subsequent replacement of another lower extremity joint.[62,64] Chitnavis and collaborators (2000) investigated 402 patients undergoing total hip or knee replacements, and reported 70% of those who received a hip replacement had radiographic evidence of OA in the contralateral hip and nearly two-thirds of those who received a knee replacement had radiographic evidence of OA in the contralateral knee.[79] Research conducted on individuals with unilateral hip OA of KL grades <III demonstrated a reduced sagittal plane knee range of motion and an increased toeing-out angle on the ipsilateral limb, suggesting a 39% chance of experiencing a shift in medial-to-lateral joint load distribution in the knee joint of the affected limb.[80] While this shift

doesn't necessarily indicate an increased risk for knee OA, it is suggested that if disease progresses to the point of having to undergo a joint replacement, the redistribution of the load after surgery exposes the medial knee compartment to joint loads it is not conditioned to and may lead to the progression and development of OA in the ipsilateral knee.[80]

Given these data, it is not surprising that joint replacement surgeries are on the rise. In Canada, OA accounts for 95% of all hip and knee total joint arthroplasty procedures.[81] From the years 2016-2017, almost 56,000 hip replacements and more than 67,000 knee replacements were performed, representing an increase of 17.8% and 15.5% respectively over the last five years.[82] Recent literature by Inacio et al. (2017) projects the number of total knee arthroplasty (TKA) procedures in the United States is expected to increase 143% by 2050, translating into 1.5 million cases per year.[83] With these rapidly increasing rates, one cannot help but wonder how resources will be obtained to maintain the delivery of necessary care to these patients.

OA is a heterogeneous disease with implications at the anatomic, molecular, and physiologic levels. As there is no current cure, OA has significant repercussions on the health and wellness of Canadians and is the culprit of many emotional, economical, and physical encumbrances. The next section will expand upon economical and physical liabilities, focusing on the individual and national effects of OA.

2.2 Burden of OA

2.2.1 Economical Burden

Osteoarthritis is an economic burden at both the community and national healthcare levels. The annual cost of arthritis in Canada is estimated to be over $7.6

billion,[84] with the cost per Canadian patient over $811 per year.[10] Direct expenses associated with OA include visits to health professionals, prescription costs, hospital stays including joint replacement surgeries, imaging and radiology, community care services, health science research, health-related pensions and benefits, and health administration.[5] Still, these estimates do not consider additional costs that may be associated, as adults diagnosed with OA are twice as likely compared to those without OA to develop at least one other chronic health condition.[1,22] A recent meta-analysis by Calders et al. (2018) revealed in individuals with hip and/or knee OA, having at least one comorbidity, such as diabetes or cardiac disease, was significantly associated with deterioration of symptoms and physical functioning, consequently creating barriers for receiving appropriate care and leading to progression of the disease.[85]

Living with OA can produce significant financial stresses impacting both the affected individual and their family. Rarely factored into cost estimates for OA are out-of-pocket expenses such as special diets, home environment modifications, use of domestic help, as well as non-prescription medications.[5] Furthermore, over 220,000 workers are living with moderate-to-severe disability as the result of OA,[1] with over half reporting absentness and over a third reporting reduced work hours.[7,8] By 2031, OA is estimated to cost the Canadian economy 17.5 billion dollars per year in lost productivity as it forces greater numbers of people to stop working or work less.[9]

It is certain the economic burden of OA has implications at both the individual and national levels. It remains unknown how the Canadian health care system is going to adjust as burdens continue to rise while life-expectancy increases, patient population physical activity levels decrease,[1,73] and access to timely health care remains limited.[1,86]

2.2.2 Physical Burden

Osteoarthritis is a significant culprit affecting physical function and independence.[20,21] Individuals with knee and hip OA often show characteristic patterns of decline in the functional mobility of their lower extremities, and consequently a degeneration in their ability to execute activities of daily living.[6] One in four older adults have been found to report walking difficulty, with the greatest effect stemming from OA of the hip and/or knee. Moreover, the likelihood of reporting walking difficulty in these individuals increased significantly with each additional knee or hip involved.[22] With symptoms such as pain and stiffness, one can understand the tendency to avoid movement. This creates a vicious cycle as lower physical activity levels and diminished quality of life associated with the disease leads to a progressive worsening of disability, and thus symptoms, resulting in less motivation to exercise.[87] Current guidelines suggest all OA patients should be encouraged to consider some form of exercise as a central part of their treatment plan, with the type of physical activity matched to the individual's personal preference, affordability, and access.[13] Current physical activity recommendations for older adults (65 years +) include accumulating at least 150 minutes of moderate to vigorous physical activity each week, along with muscle strengthening activities at least twice per week, and incorporating activities that challenge balance.[88] Despite these guidelines, studies reveal persons with OA are particularly inactive.[89–91] Farr and colleagues (2008) reported only 30% of knee OA patients who wore accelerometers for one week met Centers for Disease Control and Prevention and American College of Sports Medicine guidelines for physical activity, recommending a minimum of 30 minutes/day of at least moderate-intensity five days a week.[73]

Additionally, over 60% of individuals with OA report sedentary behaviours during leisure time.[92] This immobility translates into an increased risk for morbidity and even mortality, as a result of secondary obesity, osteoporosis, and cardiovascular risks.[87]

The burden of OA is increasingly troublesome on individuals, the overall health care system, and the economy. In order to determine how to minimize the economical and physical effects of this disease, a more in-depth understanding of the impact it has on mobility is needed.

2.2 Mobility and Gait

The International Classification of Functioning, Disability and Health (ICF) model developed by the World Health Organization (WHO) provides a multi-dimensional theoretical framework for investigating and classifying diseases and disabilities from a biological, societal, and personal perspective.[93] Human functioning is broken down into three levels: i) body/part, ii) whole person, and iii) whole person in a social framework. The influence of contextual factors, including environmental (i.e. physical, social) and personal (i.e. physical, emotional) are recognized within the ICF and incorporated into how disability is perceived by the individuals.[93,94] The ICF can be used to comprehend the intricate relationship of illness and disease with participation in individuals with OA (Figure 2-1), as structural and functional impairments of the joint often leads to disability and illness.

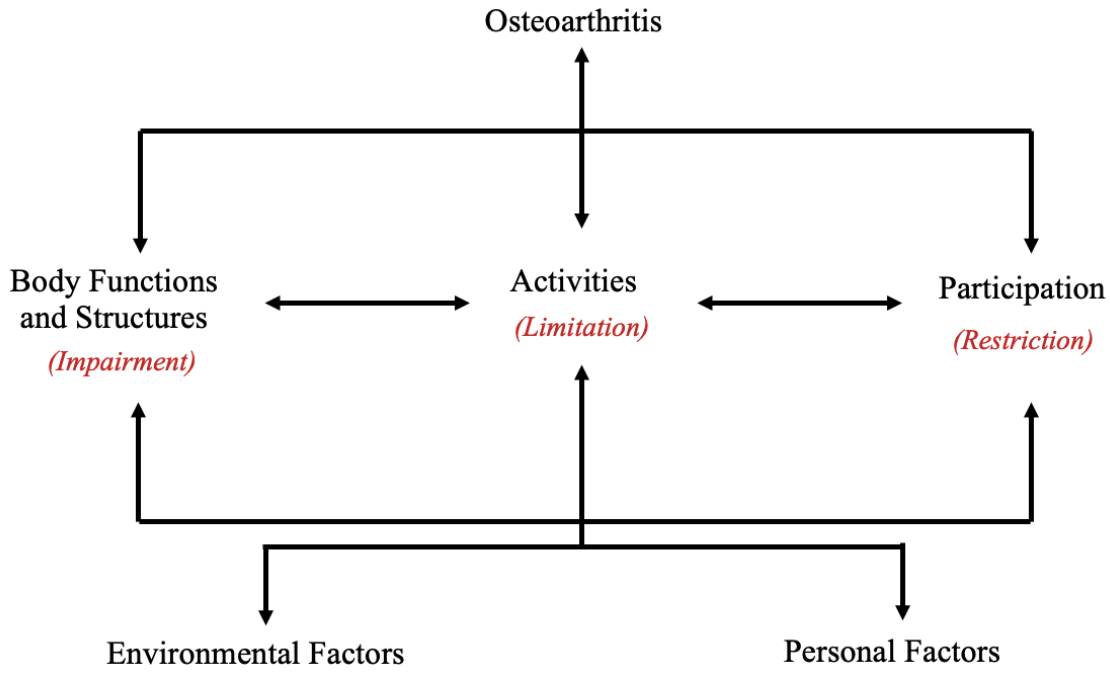


Figure 2-1. World Health Organization (WHO) International Classification of Functioning, Disability and Health.[93] *Model adapted to reflect the disease of osteoarthritis.*

The ICF considers walking as a core element in the activities and participation component of the Functioning and Disability segment.[95] The ability to walk is the single most important daily physical activity, with evidence suggesting walking ability contributes to self-assessment of one's own health in older adults.[96] Individuals with degenerative orthopaedic diseases, such as OA of the knee or hip, demonstrate considerable reductions in walking ability in comparison to healthy age-matched controls.[97] In fact, symptomatic knee and hip OA was found to be the greatest contributor to difficulty walking, and when sociodemographic factors were held constant, the presence of OA in one knee or hip increased the likelihood of walking disability from <5% to approximately 20%.[22] Consequently, with walking difficulty comes a reduction in quantity. A recent study by Sliepen and associates (2018) investigated different types and durations of physical activity among subgroups of individuals with knee OA and found

that 61 patients performed an average of 7,303 level steps per day, as measured with accelerometers worn for seven consecutive days. Although relatively close to the popular recommendation of 10,000 steps per day, 60% of participants' waking time was spent sedentary.[98]

Regular physical activity is recognized as a safe, multidimensional therapeutic treatment to improve many of the factors that result in disability in knee OA populations.[13,99] Remaining physically active has the potential to improve muscle strength, reflex inhibition, proprioception, knee range of motion and decrease the risk of excess weight gain.[99,100] There is also ample evidence that physical exercise reduces pain and enhances physical function of the OA joint.[13,90] Mesci and colleagues (2015) reported elderly patients with knee OA who are physically active had better quality of life and lower depression scores compared to their less-active counterparts.[87] Furthermore, Stubbs and associates (2015) found positive associations between physical activity with lower limb function and faster gait speed in adults with knee OA.[91]

With the ICF allocating importance on mobility and walking in individuals with OA, it is essential to understand the role of joint mechanics throughout the disease process[16,35,101,102] and the reciprocal relationships that exist between joint impairments and walking limitations. Structural tissues of the lower extremity can be conditioned, by cyclic loading, and loading can impact structural tissues, making human gait the ideal model to study joint function in individuals with lower extremity OA.[102] Biomechanical and electromyographic analyses have become a useful tool to uncover irregularities during gait and to aid in our understanding of mechanical influences on the initiation and

progression of the disease.[16,23,28,33,103] The next section of this review will look at gait mechanics, including both kinematics and kinetics.

2.3 Joint Mechanics During Gait

Contemporary methods of gait analysis often include measurements of joint kinematics and kinetics paired with the simultaneous recording of muscle activity[104] and have given rise to observational tools and techniques allowing objective evaluations of spatiotemporal parameters and three-dimensional biomechanics of human gait.[105] While mechanics play a role in the initiation and progression of OA, not enough is known about which specific mechanical parameters are most important and what their impact is on the disease process,[18] leading to an eruption of different methods and metrics regarding OA gait analyses. This section will first detail biomechanical and neuromuscular gait outcomes that have been shown to impart an understanding of knee mechanics associated with severity and progression of knee OA. These include sagittal and frontal plane moment outcomes, and differential knee joint muscle activation features. This will be followed by a review of the literature pertaining to how hip OA affects ipsilateral knee mechanics.

2.3.1 Knee OA Joint Motion

Kinematics is a branch of mechanics that describes the movement of objects through space and time, including linear and angular velocities, displacements, and accelerations.[106] Kinematic measures can explain how the bones that make up joints move relative to each other and yield information about where loads are being transmitted through the joint surfaces.[18]

In knee OA literature, the most frequently identified alterations in joint motion occur in the sagittal plane. In comparison to healthy controls, individuals with knee OA tend to walk with what is described as "stiff knee gait"[31] and this tends to be more pronounced as severity increases.[23] Individuals with knee OA appear to strike the ground with their knee in a more flexed position,[24,25,30] demonstrate a reduction in peak knee flexion angles during the loading response,[23,26–28,50] and show a reduced knee flexion excursion during the stance phase of the gait cycle including the range of motion from initial contact to peak stance flexion, and from peak stance flexion to terminal stance extension.[25,28,107,108]

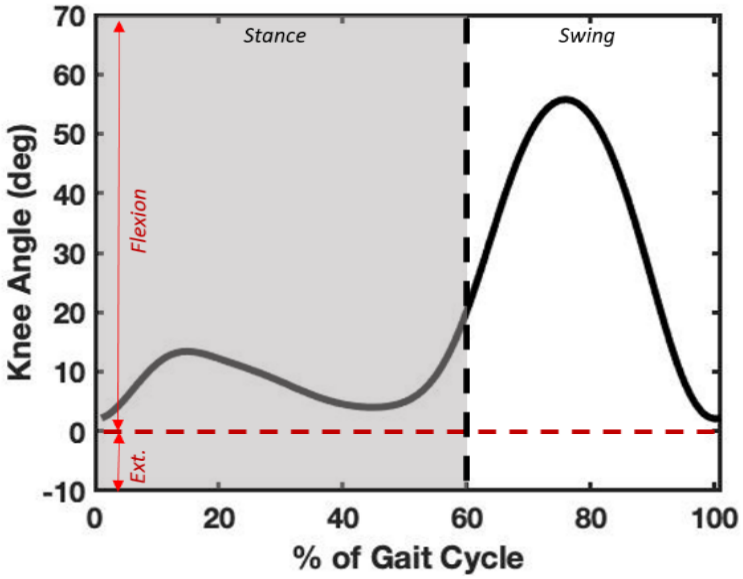


Figure 2-2. Example of sagittal plane knee joint motion in degrees throughout the gait cycle where stance phase (60% of gait cycle) is represented in grey, and swing (40% of gait cycle) is in white. Flexion is represented as being positive and extension is negative, as demonstrated by the red arrows.

During the stance phase of gait in healthy subjects, the knee is positioned near zero degrees of flexion at initial contact and moves into a position of flexion throughout the loading phase. The amount of knee flexion decreases as the body moves over the support limb during mid-stance. As the limb transitions through terminal stance, the knee

begins to extend once again nearing zero degrees of flexion during push off.[109] In an osteoarthritic knee, the joint is in a more flexed position at the time of heel strike and moves less throughout the loading response and stance phase, resulting in a "stiff" movement pattern. This reduction in knee joint excursion is suggested to be a strategy to maintain joint stability and function.[110]

Angles in the frontal and transverse plane have also been investigated;[110–114] particularly varus thrust[55–57] that has implications for understanding OA progression. There are limitations to the interpretation of these movements given methodological considerations, including soft tissue artifact and the kinematic cross talk influence of processing methods.[115–118] Sagittal plane movements have also been shown to be more reliable, particularly the range of motion measures (over absolute angles) where minimal detectable change (MDC) values for frontal plane angles may be greater than differences shown to exist between groups.[119] While sagittal plane kinematic alterations associated with knee OA remain rather consistent, little is known about their uniqueness to the disease. In fact, whether these alterations are distinctive of knee OA or of a lower extremity pathology in general remains unknown. Evidence gathered from research involving individuals with hip OA, would suggest similarities exist between these two lower extremity joint diseases.[36,38,39,66] Given kinematics is limited to understanding motion outcomes, joint moments and electromyography have been used to glean information on forces associated with motions, providing a comprehensive investigation of knee joint function, possibly linked to isolated joint dysfunction.

2.3.2 Knee OA Joint Moments

Mechanical forces have been identified as one of the most important environmental factors responsible for joint homeostasis.[120] During normal gait, forces transmitted across the knee joint range between two-to-three times an individual's body weight,[121] with the risk of knee OA increasing by 35% with each 5 kg/m^2 increase in body mass index (BMI).[122] In general, measures of *in vivo* forces transmitted by lower-extremity joints are not commonly attainable, and therefore are estimated using surrogate measures.[40] External moments occurring about the joint centers are frequently used to evaluate joint loading and are often computed through inverse dynamics analysis. Using this method, a combination of anthropometric measures, segment kinematics, ground reaction forces (GRFs), joint center locations, and equations pertaining to linked segment modelling are used to identify the resultant joint forces and moments that cause acceleration of body segments.[123,124] These calculated joint forces and moments are equal and opposite to the net internal forces and moments generated by muscles crossing the joint, surrounding soft tissues, and contact forces.[30] The following paragraphs will focus on the sagittal and frontal plane knee joint moments and how they have allowed us to understand pathomechanics associated with knee OA gait in comparison to an asymptomatic group of individuals.

2.3.2.1 Sagittal Plane Moments

While the KAM is the most common measure for estimating medial tibiofemoral contact force,[40,125,126] approximately 85% of the work performed during gait occurs in the sagittal plane[127] and therefore it is not surprising the flexion-extension moment has also demonstrated to be predictive of peak joint loading.[102] The external flexion-extension

moment is reflective of all agonist and antagonist muscles crossing the knee joint[40] and has shown to differ between asymptomatic, moderate, and severe knee OA groups.[23]

Individuals with knee OA have been reported to walk with reduced early stance flexion moments[23,128] and terminal stance extension moments.[25,41,129] Asay and colleges (2018) conducted a study on the relative contributions of frontal and sagittal plane knee joint moments in 19 individuals with medial compartment knee OA with a KL grade of >I and followed up five years later to evaluate the change over time. Results suggested a shift in domination of the total knee joint moment from knee flexion moment at baseline, to KAM at five-year follow up.[130] Interestingly, Chehab and colleagues (2014) also conducted a longitudinal study with a five-year follow-up on 16 individuals with medial compartment knee OA with a KL grade of >I where they investigated the association between peak KAM and flexion moments and knee cartilage changes. Their results suggested while both baseline peak knee flexion and adduction moments were associated with changes in the tibial medial-to-lateral thickness ratio and medial cartilage regions, these associations were primarily dominated by the knee flexion moment. Results of the regression analysis showed that a 1% Body Weight*Height increase in the peak knee flexion moment indicated an average reduction of 0.06 units in the tibial medial-to-lateral cartilage thickness ratio and an average loss of 0.15mm in medial tibial cartilage over five years.[45] Together these results suggest the peak knee flexion moment plays a role in disease progression and gait adaptations to reduce the impact have been identified in individuals with knee OA.

While discrete metrics of the knee flexion moment are commonly reported in the literature, results of a recent reliability study by Rutherford and colleagues (2020)

conducted on healthy participants during treadmill walking demonstrated absolute peak flexion and extension moment reliability was lower than when the range from peak flexion to peak extension moments were calculated.[119] This aligns with research by Brisson and colleagues (2018), who demonstrated questionable intraclass correlation coefficients (ICC) (0.48-0.52) for peak knee flexion moment and suggested fluctuations in this metric may be partly due to gait speed.[131]

Several researchers have investigated the range between peak flexion and extension moments rather than the discrete metrics. Hatfield and colleagues (2015) conducted a population-based study on 80 participants with moderate medial compartment knee OA, 54 of which were able to follow up five-to-eight years later and report whether they underwent a TKA or not. Baseline gait analysis results revealed a reduction in the knee flexion-extension moment range in the TKA group compared to those who did not undergo a TKA.[31] Similarly, Rutherford and collaborators (2017) investigated the effect of age and knee OA on knee joint biomechanics where they compared 20 young adults, 20 older adults, and 40 individuals with knee OA.[28] They reported individuals with knee OA demonstrated less difference between peak flexion and peak extension moments compared to healthy older adults. This reduction in range is suggested to coincide with what has been described above as "stiff knee" gait[31,50,132] and is thought to be an adaptive strategy to overcome knee joint instability as structural degradation progresses through elevated agonist and antagonist muscular activation.[23,24,50,129,133,134]

2.3.2.2 Frontal Plane Moment

As previously mentioned, a particularly important biomechanical measure in knee OA literature is the KAM, as it represents the magnitude of intrinsic compressive load distribution between the lateral and medial tibiofemoral knee compartments.[30,34,41] During walking, the net GRF passes medial to the knee joint center in the frontal plane, resulting in a KAM that rotates the tibia medially on the anterior-posterior axis of the knee joint.[135,136] In a normal state, up to 80% of total forces transmitted across the knee are placed on the medial tibiofemoral compartment during gait[137] as the adduction moment is larger than the abduction moment, suggesting a greater medial compared to lateral compartment loading. Kutzner and colleagues (2013) conducted a study of individuals with instrumented total knee replacements and reported the KAM has been related to in vivo medial compartment loads (R^2=0.51-0.76) and is an appropriate surrogate measure for predicting the medial force ratio throughout various aspects of the stance phase of gait.[135]

Dynamic joint loading, as measured by the KAM, has been associated with knee OA disease severity for decades.[23,34,42–45] For example, Sharma and colleagues (1998) reported greater peak KAM with advancing stage of medial knee OA, whether disease severity was assessed as narrowest joint space width or by KL grade, and persisted even after controlling for age, sex, and pain.[34] Miyazaki and associates (2002) tested whether the peak KAM could predict radiographic progression of medial compartment knee OA at six-year follow up using logistic regression analysis and reported the risk of knee OA progression increased 6.46 times with a 1% increase in peak KAM.[43] More recent literature has reiterated this association, as Hatfield and colleagues (2015) used Principal Component Analysis (PCA) to determine if biomechanical gait patterns differed between

those moderate knee OA patients who progressed to TKA, and those who did not. They found the TKA group to have higher KAM overall magnitude than the no-TKA group at baseline.[31]

Previous work has also identified differences in frontal plane loading between individuals with moderate knee OA and asymptomatic controls. Baliunas et al. (2002) investigated biomechanical responses during gait of 31 individuals with moderate knee OA and demonstrated they had an increased peak KAM compared to asymptomatic individuals.[30] This research was supported with findings by Astephen et al. (2008) who identified an increase in mid-stance KAM in both moderate and severe knee OA populations compared to age-matched symptomatic controls.[23] Furthermore, Rutherford and colleagues (2017) compared biomechanical metrics between individuals with moderate knee OA to both asymptomatic older and younger adults and reported the knee OA participants had an increased peak KAM compared to healthy older adults, however had comparable frontal plane loading to the younger asymptomatic adults.[28] This supports the notion that healthy and diseased cartilage respond differently to physiological loading.[28,103]

Although the discrete measure of peak KAM has shown to be related to knee OA presence and progression, it only measures the load at one instance of the stance phase of gait and thereby does not consider the duration of joint loading. A more comprehensive measure may be the KAM impulse, which considers both the magnitude of the load and the duration of the stance phase.[44,138,139] Thorp and colleagues (2006) were one of the first groups to measure KAM impulse in knee OA and reported that both peak KAM and KAM impulse increased with increasing severity, however only KAM impulse differed

between mild and moderate knee OA groups.[140] Since then, several more recent studies have also associated KAM impulse with structural disease progression.[44,141,142]

Previous work by Robbins and Maly (2009) examined the changes KAM in response to controlled changes in gait speed in healthy individuals during overground walking and reported changes in peak KAM and KAM impulse as the result of different walking speeds occur in opposite directions; during slow gait, the KAM impulse increases, whereas during fast gait the peak KAM increases. The KAM impulse increases during slow gait speeds because the stance knee is exposed to medial loading for a longer duration of time, as well as the KAM waveform displays less of a reduction in magnitude between the two peaks, resulting in a greater area under the KAM curve. Peak KAM increases during fast gait speeds as the result of an increased vertical ground reaction force. Considering both measures represent different characteristics of medial knee loading, it is suggested both be examined when analyzing the KAM.[139]

Frontal plane moments give researchers an idea of the medial-to-lateral load distributions present within the knee joint during gait. The KAM is the most commonly reported measure in knee osteoarthritis literature and has been consistently linked to both presence and progression of medial knee OA. Osteoarthritic knees demonstrate an increase in peak KAM both in comparison to asymptomatic controls, and with increasing disease severity. The KAM impulse provides additional information about the duration of the medial compartment knee load and has also been associated with structural disease progression. However, these metrics only provide information about one plane, and as gait is a multi-dimensional movement, analyzing the flexion and adduction moments together may provide a better assessment of joint loading.

It is clear from the literature that differences exist in the sagittal and frontal plane knee joint moments between both OA and asymptomatic groups, and throughout the progression of the disease. Increased peak KAM, as well as less dynamic flexion-extension moments are reliable measures[119,143,144] and have been consistently associated with the presence and progression of knee OA. While these biomechanical variables provide an indication of the external forces acting on the knee joint, the equations used to calculate net joint moments do not account for muscle contributions causing the motion. Therefore, it is important to consider the activation of the musculature surrounding the knee joint to gain a more complete picture of the dynamic joint environment in individuals with OA.

2.3.3 Knee OA Joint EMG

While OA is typically described as a disease of joint structures, there are several key elements working together to preserve joint function. Panjabi (1992) proposed a model for understanding joint stability that was comprised of three interacting subsystems; the first being the passive (ligamentous) subsystem, whose nomenclature is based upon ligaments inability to generate motion by themselves. Nevertheless, ligaments are dynamically active as transducers in the neural control system, which is the second subsystem of Panjabi's model. This system receives information from the various sensors of the body, determines the appropriate stability requirements, and activates the third and final component, the active (musculotendinous) subsystem, to achieve the stability goal. The active system is comprised of muscles and tendons and are the means through which stability and movement are accomplished.[145] During gait, all three systems are operating to establish a balance between joint stability and mobility and can be affected by injuries

and disease of the involved joint. Determining how neuromuscular activations differ between individuals with and without comprised knee joint function may help achieve a better understanding of the altered mechanical environment present in OA joints.[46]

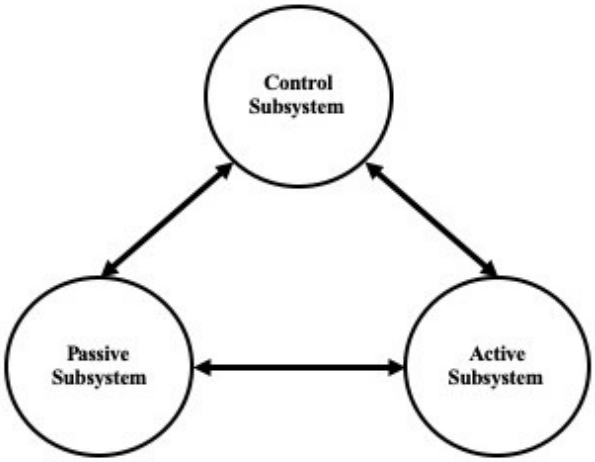


Figure 2-3. Panjabi's model of the interacting passive, active, and control subsystems for stability. Adapted from Panjabi (1992).[145]

Neuromuscular activations during gait are typically measured through surface electrodes placed over the muscles of interest and displayed as EMG waveform data. Determining how these signals fluctuate across phases of the gait cycle and how they correspond to changes in joint mechanics allows for interpretation of the demands placed on the joint during walking. To date, many studies employing EMG either using discrete amplitude or pattern recognition analysis, have suggested a "stiff knee" gait strategy is present in individuals with knee OA and is thought to be an adaptation to counteract increasing stability demands.[24,28,31]

2.3.3.1 Hamstring Activation

The hamstring muscle group is comprised of the semitendinosus, semimembranosus, and biceps femoris muscles located in the posterior thigh. Together, they are primary flexors of the knee joint, extensors of the hip,[146] and contribute to

dynamic knee joint stability.[147] Along with the quadriceps, they are suggested to have a direct impact on compartmental loading of the knee through differential activation of the medial and lateral muscles crossing the joint. [147,148]

Increased overall LH amplitudes are the most consistently reported neuromuscular adaptation reported in individuals with knee OA compared to asymptomatic individuals.[28,46,47,51] Hubley-Kozey and colleagues (2006) used PCA to identify significant principal neuromuscular patterns between asymptomatic and moderate medial knee OA groups, and found significantly higher muscle activity amplitude, for the Maximum Voluntary Isometric Contraction (MVIC) normalized LH activity in the OA group compared to the MH, and both hamstring muscles for the control group. The LH activity peaked prior to initial contact, decreased during the first 10-15% of the gait cycle, and increased again around 85% of the gait cycle.[46] This research is supported by findings by Sharma et al. (2017) who described a similar muscular activation pattern for the hamstring muscles in individuals with knee OA compared to an asymptomatic cohort.[149] Lateral hamstring activity has also shown to increase progressively in amplitude with increasing knee OA severity.[23,47,150] Rutherford and colleagues (2013) used PCA to compare neuromuscular activations among individuals with moderate knee OA stratified by KL grade and identified greater overall MVIC normalized LH amplitudes with increasing structural impairment, suggesting the lateral musculature may be recruited to provide greater active stiffness to the joint as the KL grade increased.[150] These discoveries indicate the LH may be influential in the knee OA process, however whether these alterations are a predecessor, or a consequence, remains unknown.

In contrast to the LH, discrepancies exist regarding MH alterations coinciding with knee OA. Several studies have reported MH amplitudes to be unaffected by knee OA. Hubley-Kozey and colleagues (2006),[46] as well as Rutherford et al. (2010),[151] found statistically similar MVIC normalized MH activation amplitudes between knee OA and asymptomatic groups of participants. In contrast, Astephen-Wilson and associates (2011) described increased MVIC normalized MH amplitudes throughout early-to-mid stance in individuals with increasing pain severity in knee OA participants.[152] Inconsistencies among studies could be ascribed to differences in sample sizes, gait velocities,[52] as well as differing pain[46,151] and strength levels among participants.[48]

Lateral hamstring activity not only appears to be elevated in between group comparisons, but within subject analyses have revealed further imbalances exist between the LH and MH in individuals with medial compartment knee OA. Current findings suggest that individuals with mild-to-moderate medial compartment knee OA selectively recruit their lateral musculature during early and mid-stance with greater amplitudes and for longer durations than their medial musculature.[46,49,53] Lynn and associates (2008) computed a medial: lateral hamstring % MVIC activation ratio by averaging EMG activation across the entire stance phase for both muscles then dividing the medial activation level by the lateral.[49] An alternate ratio was calculated in a recent study by Rutherford and Baker (2019), where raw medial and lateral root mean squared (rms) amplitudes over the entire gait cycle were computed and the medial activation value was subtracted from the lateral.[53] Results of both studies revealed a bias towards greater LH activity, further iterating individuals with knee OA favor activation of the LH over the MH during walking. Imbalances between LH and MH activity has also shown evidence

linking to disease severity. Rutherford et al. (2011) reported greater MVIC normalized LH activation compared to MH in individuals with severe knee OA (TKA candidates) compared to both moderate knee OA (non-TKA candidates) and asymptomatic groups.[51] This explicit differential activation has not been reported in asymptomatic adults,[46] the contralateral knee of knee OA patients,[58] nor younger adults or those with hip injuries,[59] and thus may be unique to knee OA pathology and provide information regarding disease progression.

The occurrence of elevated LH activity in individuals with knee OA is thought to be related to the presence of articular cartilage degeneration in the medial compartment. Various mechanical explanations have been proposed, including i) to assist in unloading the medial knee compartment,[46] ii) a response to lateral compartment tensile stress,[25,46] and iii) a result of the LH having a smaller cross-sectional area in comparison to the MH.[153] Despite these explanations, the exact mechanism behind the elevated hamstring activity present in individuals with knee OA remains unknown.

2.3.3.2 Quadriceps Activation

The quadriceps muscle group is comprised of the vastus medialis (VM), vastus lateralis (VL), rectus femoris (RF), with the vastus intermedius lying beneath RF, in closer proximity to the femur.[154] They assist in controlling the knee joint throughout motion and are responsible for generating knee extension and hip flexion. During gait, the role of the quadriceps femoris muscles is to control knee joint flexion during weight acceptance while the hamstrings and gastrocnemii remain rather silent.[29]

Unlike the hamstrings, several studies have reported individuals with knee OA to execute a global activation of the quadriceps, thereby increasing both VL and VM

simultaneously throughout the gait cycle.[29,47,150] Hubley-Kozey and colleagues (2009) investigated co-activation differences in the lower extremity muscles of individuals with varying severities of knee OA, and reported those with severe knee OA, as defined by their KL grades of III or IV, inability to meet functional criteria, and eligibility for total knee replacement surgery, demonstrated elevated activity in both VL and VM muscles throughout most of the stance phase in comparison to both individuals of lesser disease severity (moderate OA), and asymptomatic controls.[47] This finding is supported by work by Rutherford and associates (2013) where individuals with knee OA were stratified by KL grade into minimal (KL II), moderate (KL III), and severe (KL IV) structural impairment, and compared to age-matched asymptomatic controls. Authors reported greater overall quadriceps muscle activation amplitudes in all three OA groups in comparison to the asymptomatic group, with the KL IV group demonstrating the highest activity levels throughout the stance phase. No significant differences in activation between VL and VM were reported for any of the groups.[150]

In contrast, Hubley-Kozey and colleagues (2006) reported higher VL recruitment for individuals with moderate OA compared to controls, and similar VM recruitment amplitudes between asymptomatic and OA groups using PCA.[46] Similarly, in the later 2009 publication, Hubley-Kozey et al. reported increased VL activity in the moderate knee OA group, defined by KL grades I-III, ability to meet functional criterion, and who were undergoing conservative treatment, in comparison to the healthy controls. [47]

Together these data suggest quadriceps activity increases with the presence and progression of knee OA, however the greater VL to VM activity has not been a consistent finding and may be associated with differing disease severities.

2.3.3.3 Gastrocnemii Activation

While often associated with movement at the ankle, the gastrocnemius muscle is a strong flexor of the knee and has a significant role during the propulsion stage of the gait cycle.[155] Like the other lower extremity muscle groups, the gastrocnemii have also shown neuromuscular alterations with the presence of knee OA. In comparison to asymptomatic controls, Hubley-Kozey and associates (2006) reported overall amplitude reductions in the medial gastrocnemius (MG) in individuals with moderate knee OA, such that they recruited both medial and lateral gastrocnemii (LG) to a similar percentage of MVIC, whereas the asymptomatic group recruited MG to a higher percentage of MVIC, coinciding with its larger cross-sectional area.[46]

In contrast, Rutherford and colleagues (2011) did not find significant differences in overall amplitudes of gastrocnemii activity between groups of moderate knee OA, severe knee OA, and asymptomatic participants.[51] However, both Hubley-Kozey et al. (2006) and Rutherford et al. (2011) reported an earlier increase in MG activation compared to LG, in asymptomatic individuals and individuals with moderate knee OA as identified using PCA.[46,51] It appears those with severe knee OA may not demonstrate this shift in activity, instead, a reduced late stance to early stance activity was reported compared to asymptomatic and moderate OA groups.[51] Severe OA participants showed higher early stance activity in both MG and LG, however only MG had decreased activity during late stance.[51] The heightened activity during early stance may provide active stiffness to increase joint stability during the period of weight acceptance and single limb support.[51] On the contrary, the reduced MG activity during late stance adopted by individuals with knee OA may be an attempt to reduce medial joint loading. [46]

Several studies have investigated the role of the gastrocnemii muscles in the context of co-contraction.[25,133] Lewek and colleagues (2004) demonstrated a higher medial muscle (VM and MG) co-contraction index (CCI) from the period of 100ms prior to initial contact to the time of peak KAM in individuals with knee OA who display genu varum alignment compared to healthy controls. This increase in medial muscle activity was associated with localized medial joint laxity in the individuals with knee OA and thought to be a response to stabilize the medial side of the joint.[133] On the contrary, Heiden and associates (2009) grouped the gastrocnemii with hamstring and quadriceps muscles to develop a medial (MH, VM, MG)/lateral (LH, VL, LG) muscle co-contraction index across the stance phase in individuals with knee OA compared to an asymptomatic group. Results of their study demonstrated knee OA patients having greater lateral muscle activity in loading and early stance whilst the controls had greater medial activity. Then in mid-stance, the OA patients tended to utilize the medial and lateral muscles equally whilst the controls experienced high levels of medial muscle activity.[25] While the direct contribution of the MG and LG is hard to determine given the nature of the CCI, together these data suggest the gastrocnemii muscles play a role in the knee OA environment.

In conclusion, previous findings have identified biomechanical and neuromuscular alterations coinciding with knee OA presence and progression. However, the uniqueness of these parameters to knee OA exclusively remains unclear, as individuals with hip OA have presented several similar alterations during gait, including altered knee joint motion,[67,80,156] and neuromuscular activations.[66,67] Identifying which mechanical features are specific to knee OA is essential to understand the true extent of

the disease on joint function, leading to the development of effective intervention plans and enabling clinicians to better understand, assess, and treat knee OA.

2.3.4 Joint Mechanics in Hip OA

While the above biomechanical and neuromuscular adaptations associated with knee OA presence and progression remain rather consistent, little is known about their uniqueness to the disease. In fact, whether they represent pathomechanics distinctive of knee OA exclusively or of a lower extremity pathology in general remains unclear. Osteoarthritis in either the hip or knee has been suggested to alter the hip-knee-ankle kinetic chain in a way that influences the risk of both symptoms and structural changes in other lower extremity joints.[157,158] In fact, epidemiological studies have shown that a significant number of OA patients have pathologies in several of the bearing joints, suggesting that problems in one joint may be biomechanically related to problems in others.[60,61]

The effects of hip OA on hip joint biomechanics are well documented in the literature,[35,38,159,160] however an understanding of knee joint mechanics in this population is lacking. A majority of studies investigating changes in the knee joint are limited to patients at later stages of the disease or post-operative populations,[63,64,161] resulting in an incomplete picture of the impact of hip OA on knee mechanics in individuals who are not candidates for THR.

Hip and Knee Joint Motion

The most common kinematic alteration during gait in individuals with hip OA is reduced extension during terminal stance.[35–39,160] This reduction has been found to become greater as hip OA severity increases.[36,160,162] Coincidently, at the same point in

the gait cycle, the knee joint is moving into extension as the ankle joint is dorsiflexing[163] which creates the environment for limitations at the hip joint to impact ranges of motion at distal segments.

Regarding knee kinematics, Rutherford and colleagues (2015) conducted a study on individuals with moderate severity unilateral symptomatic hip OA (not THA candidates) who reported no limitations with walking a city block, climbing stairs, and jogging >5 meters, and compared knee joint mechanics to an age-matched asymptomatic population. Results of their study showed no significant between-leg differences for sagittal plane knee joint motion for either group, however a significant group interaction was reported for the range of motion from peak flexion to peak extension during stance phase where individuals with hip OA demonstrated a 5-degree reduction in range.[66] Similar findings were reported by Eitzen and associates (2012) in their study including individuals with hip OA reporting mid-to-moderate symptoms as determined by a score of 60-95/100 on the Harris Hip Score (higher score indicates better outcome) in comparison to asymptomatic participants. Individuals with hip OA showed a reduction in ipsilateral knee joint extension during the latter 50% of stance phase, where 4-to-9-degree differences were reported in comparison to the controls.[39] Together these results demonstrate that as the knees of individuals with hip OA transition from peak flexion to peak extension during mid-to-late stance, they remained in a flexed position and do not move fully into extension. This reduction in range has been demonstrated in individuals with knee OA in comparison to asymptomatic controls[23,28,32] and is associated with the "stiff knee" gait mentioned above.

This decrease in sagittal plane knee joint motion appears to be more pronounced in the ipsilateral, rather than contralateral limbs of individuals of moderate and severe hip OA. As captured using PCA, Rutherford and collaborators (2018) reported a less dynamic knee joint motion (i.e. less differences between loading response, later stance, and swing angles) in individuals with severe hip OA (THA candidates) in comparison to those with moderate hip OA (non-THA candidates), which was more pronounced in the ipsilateral than contralateral limbs. These data suggest that with increasing disease severity, the ipsilateral knee becomes less dynamic throughout the gait cycle.[67] These findings coincide with research investigating sagittal plane range of motion throughout knee OA disease progression, where individuals with advanced disease display less knee joint range of motion in comparison to those of moderate disease severity[27] and asymptomatic controls.[23,164]

While individuals with hip OA often present with a reduced hip joint range of motion, made up largely of restrictions during terminal stance, knee kinetics also appear to be affected in some samples. Joint motions provide an outcome of underlying physiological processes of which forces, may play a role. Joint moments can be used to further understand the impact of hip OA on knee joint mechanics.

Knee Joint Moments

Shakoor and associates (2003) conducted one of the first studies aimed to identify asymmetries in dynamic loading of the knee in participants with end-stage hip OA and found these patients to exhibit increased peak KAM in the contralateral knee compared to the ipsilateral knee at the pre-operative stage.[63] Since then, several studies have also identified abnormal loading factors in the contralateral knee compared to the ipsilateral

limb at severe stage of the disease.[80] However, the loading environment of the knee joint early on in the disease process still remains unclear.

Only a few studies have focused on how earlier stages of hip OA affect loading at the knee.[38,39,66,67,165] Shakoor et al. (2011) aimed to detect early asymmetries in knee joint loading by investigating individuals with unilateral hip OA who did not have symptoms of knee OA. Results demonstrated heightened peak KAM, total medial compartment knee loads, and peak knee flexion moments at the contralateral knee relative to the ipsilateral knee, suggesting an increased risk of developing progressive symptomatic knee OA in the contralateral limb.[166] While several studies have re-iterated this increased risk in the contralateral limb,[62–65] few have focused on the implications of altered knee joint loads in the affected limb and how it may help us understand early OA joint mechanics.

Schmidt and colleagues (2017) conducted a study comparing gait mechanics of 18 individuals with unilateral hip OA (KL grade >3) and 18 age, sex, and height matched healthy controls and reported a reduction in the second peak of the KAM in the affected limb in comparison to the non-affected limb and healthy controls. This reduction in second KAM indicates a shift in medial-to-lateral load distribution in the ipsilateral knee during the second half of stance phase.[80] A similar study by Steif and associates (2018) investigated knee joint loads in individuals approximately 2 years after THA in comparison to healthy controls and reported the alterations in second KAM of the ipsilateral knee previously reported by Schmit et al., (2017) persisted two years post-op.[156] This medial-to-lateral shift suggests a transfer of load to a region of cartilage not conditioned over time and thus may initiate a degenerative pathway of the lateral compartment of the knee.[156]

Together, literature supports that knee biomechanics are altered in the ipsilateral and contralateral knees of individuals with hip OA despite having asymptomatic knees. Some of these findings align with isolated knee OA findings, thereby bringing into question the uniqueness of altered knee mechanics in knee OA. Biomechanics only provides a portion of the picture of knee joint function. In many studies, including those investigating knee function in knee OA, muscle activation levels and patterns have been investigated as previously discussed. What is still incomplete, however, is the determination of whether previous knee OA findings are unique to the knee OA process.

Knee Joint EMG

While there is evidence of some comparable alterations in knee joint mechanics between hip and knee OA, it remains unclear if neuromuscular changes characteristic of knee OA are present in this population. Previous work on individuals with moderate hip OA have shown quadriceps activation is greater during mid stance compared to early stance, described as a prolonged activation in mid stance, which was not apparent in the asymptomatic comparison group,[66] and has shown to occur in those of more progressed disease severity.[67]

In opposition to the quadriceps, Rutherford and colleagues (2015) found no differences in peak normalized hamstring activation patterns between individuals with moderate hip OA and an asymptomatic cohort.[66] However, in a more recent study, greater peak normalized hamstring activity amplitudes were present in individuals with severe hip OA compared to those of moderate severity.[67] Interestingly, when both moderate and severe OA groups were considered, a significant muscle main effect was found where overall MH activity was greater than LH.[67] This finding is opposite to previous findings

in knee OA literature; however, results of this study were normalized to peak amplitudes rather than to MVIC amplitudes and consequently hinder the ability to compare absolute amplitudes between legs, groups, and studies. Nevertheless, more research is needed to understand how hamstring activation differs depending on the joint affected.

The similarities in quadricep and hamstring activations among osteoarthritic knees and the ipsilateral knees of those with hip OA may be a result of the alike movement pattern throughout the gait cycle. As previously mentioned, both individuals with knee OA[25,28,107,108] and hip OA[39,66] have shown a reduction in knee joint range of motion throughout the stance phase. With the knees remaining in a more flexed position during mid-to-late stance, it is possible that passive contributors to joint stability are not optimized (i.e. articular joint surface congruency, ligament tension) and therefore greater demands are placed on the active system to meet stability requirements.[145]

Only a few studies have investigated gastrocnemii activation in individuals with hip OA. Schmidt et al. (2016) examined muscular adaptations in individuals one day prior to their scheduled THR and found the mean MG activity throughout the gait cycle of the affected limb to differ in comparison to healthy controls.[167] Results of another study on individuals with hip OA who underwent THR suggested they displayed a prolonged, plateau-like activation throughout the entire stance phase whereas the control participants displayed a normal activation pattern such that activity increased until the middle of terminal stance phase.[168] The continuous MG activity throughout stance phase was thought to provide ankle stabilization,[155,168] however inferences about its effect on knee joint stability were not made.

EMG studies provide insight into the activity of the surrounding muscles and how they may be contributing to the mechanical environment of the joint. Parallels exist among neuromuscular activations in individuals with knee and hip OA, such as heightened quadricep and hamstring activity during stance, while discrepancies are present too, including biases towards medial vs. lateral differential activations. As one group of individuals has pathology in the knee joint, and one does not, further investigation is required to determine what features are distinctive of knee OA gait.

In summary, characteristic pathomechanical alterations linked to disease progression and severity have been identified in individuals knee OA, yet several of these alterations have also been reported in the knees of individuals with hip OA. Why does one group with a known knee pathology show similar mechanics to a group with asymptomatic knees and hip OA? Although research exists comparing both OA groups to asymptomatic cohorts, they have never been directly compared to each other. Identifying specific alterations unique to each pathology is crucial to continue the evolution of effective management and treatment strategies.

2.4 Reliability of Gait Outcomes

Gait analyses are a well-established tool for quantifying outcomes of lower extremity joint function and often seek to discriminate between normal and pathological gait to assess changes in walking mechanics over time.[169] A frequent concern in gait analysis procedures is the ability to detect true change from assessment associated error, as measurements with high amounts of error may lead to underestimation, or failure to detect significant differences. Knowledge of this error magnitude can enable researchers and clinicians to minimize the risk of interpreting small differences as meaningful and

have greater confidence in detecting true differences.[169,170] This section will expand upon the reliability of gait outcomes pertaining to this thesis.

Several studies have reported moderate to excellent test-retest reliability for sagittal plane kinematic outcomes during gait,[143,169] where moderate is defined as ICC values between 0.5-0.75, good as values between 0.75-0.90, and excellent as values above 0.90.[171] Meldrum et al. (2014) reported test-retest ICCs between 0.60-0.84 for peak and ranges of knee joint motion values during over ground gait in 30 healthy subjects with the standard error of measurement $<5^{o}$ for all parameters, however the ICCs were higher for the ranges of motion in comparison to the peaks.[143] This was further supported by Rutherford et al. (2020), an investigation completed in the Joint Action Research (JAR) laboratory at Dalhousie University during treadmill gait where the ICC values for the sagittal plane absolute joint angles were lower than for ranges of motion (i.e. knee ROM from max stance to min late stance), nevertheless all sagittal plane angle ICCs were over 0.70.[119] Moreover, a systematic review by McGinley and associates (2009) including 15 full manuscripts and eight abstracts including both healthy participants and individuals with gait pathologies, concluded sagittal plane motion reliability was typically higher than 0.8.[169]

Kinetic measures, including sagittal and frontal plane joint moments have also demonstrated high test-retest reliability during gait.[144,172] Birmingham and colleagues (2007) conducted a test-retest investigation of the peak KAM during walking in patients with medial compartment knee OA and reported an ICC of 0.86.[172] Similarly, Robbins and associates (2013) reported an ICC of 0.91 for the maximum KAM during early/mid stance of over-ground gait in individuals diagnosed with moderate knee OA.[144] In regard

to the sagittal plane, discrete values of maximum and minimum moment magnitudes have demonstrated ICCs ranging from 0.57-0.81,[144] however Rutherford et al. (2020) demonstrated peak flexion and extension moment reliability was lower (ICC = 0.78-0.80) than when the range from peak flexion to peak extension moments were calculated, which yielded in an ICC of 0.93.[119] This aligns with research by Brisson and colleagues (2018), who demonstrated questionable ICCs (0.48-0.52) for peak knee flexion moment and suggested fluctuations may be partly due to gait speed, leading to inconsistencies in literature linking the flexion moment with knee OA progression.[131]

Electromyographical outcomes are another frequent component of gait analysis showing high reliability. The EMG protocol described in this thesis are consistent with procedures described by Hubley-Kozey and colleagues (2013) who reported ICCs for overall muscle activity amplitudes, as captured using PCA, of the seven lower-extremity muscles included in the current study ranging from 0.73-0.97 during over-ground walking in individuals with moderate knee OA. The lowest ICC of 0.73 was reported for MG, and the highest of 0.97 for RF.[173] Furthermore, mean electromyography activity (% MVIC) outcomes were found to have ICCs of 0.74-0.97 for the same muscles in a healthy population during treadmill gait in previous work by Rutherford et al. (2020), where the lowest ICC of 0.74 was reported for VM, and the highest of 0.97 for LG.[119]

In summary, moderate-to-excellent between session ICC values have been demonstrated for discrete metrics of sagittal plane range of motion, sagittal and frontal plane moments, and neuromuscular activation amplitudes in both healthy and OA populations during gait.

Chapter 3 - General Methodology

This study is in part, funded by the Nova Scotia Health Research Foundation (NSHRF) [Grant # MED-EST-2014-9605 & MED-DI-2014-9558]. Recruitment, instrument selection and analysis procedures were approved by the Nova Scotia Health Authority (NSHA) Research Ethics Board (REB) [ROMEO # 1017467, 1017420 and 1020825]. The author of this thesis was primarily involved in leading the recruitment and collection of participants with moderate unilateral hip OA, whereas participants with knee OA and the asymptomatic individuals were part of a database at the JAR Laboratory at Dalhousie University and collected using the same standardized procedures listed below.

3.1 Subject Recruitment

3.1.1 Participants with Moderate OA

Participants with moderate medial compartment knee OA were recruited from Dr. William Stanish at the Orthopaedic and Sports Medicine Clinic of Nova Scotia and Dr. Nathan Urquhart at the Dartmouth General Hospital. Participants with moderate unilateral hip OA were recruited through Dr. Ivan Wong at QEII Health Science Center, and Dr. Nathan Urquhart. Individuals with moderate OA were diagnosed using the ACR guidelines, and consideration of radiographical evidence of OA were part of the clinical decision making. Clinical criterion for knee OA outlined by ACR include knee pain in addition to at least one of the following criteria: i) crepitus on active movement ii) osteophyte formation iii) morning stiffness $\leq$ 30 minutes iv) age $\geq$ 50.[70] The ACR clinical criterion for hip OA include: i) pain in the hip along with internal hip rotation < 15^{o} and hip flexion < 115 ^{o}, or ii) hip pain paired with internal hip rotation $\geq$ 15 ^{o},

morning stiffness ≤ 60 minutes, and age ≥ 50.[174] Eligible participants were approached by their respective doctors using a standardized introduction to the research study and given a letter with information about the study objectives. Interested participants were asked to provide written consent for a transfer of contact information, which was used by the author and fellow investigators to contact the participants by telephone using a standardized script to determine final eligibility for the study. The script was used to determine the presence of any cardiovascular, respiratory, or neurological conditions that would impair one's ability to complete study requirements and to confirm the existence of unilateral knee or hip OA. The patients were also asked to self-report their functional ability to complete the following tasks: i) walk at least one city block, ii) jog five meters, iii) climb or descend stairs in a reciprocal fashion, and iv) walk continuously for 30 minutes. These functional criteria are used to help ensure participants are of the moderate severity stage of OA[46,66] and if participants were unable to complete these tasks, they were excluded. The inclusion criteria for all OA participants were as follows:

- Age ≥50 years
- Diagnosis of OA in one knee or hip
- Not a candidate for total joint replacement surgery
- No cardiovascular disease (controlled high blood pressure acceptable)
- No neurological disease
- No existing musculoskeletal disease or injury other than knee or hip OA
- No lower limb surgery within the past year
- No previous joint replacement surgery
- Ability to walk independently without ambulatory aid
- Self-reported ability to:
    - Jog 5 meters
    - Walk more than a city block without aid
    - Climb stairs in a reciprocal fashion (i.e. one foot over the other)

3.1.2 Asymptomatic Participants

Asymptomatic participants were recruited from the local area using poster advertisements, social media, and emails. Interested individuals were sent a letter outlining the purpose and details of the study and contacted by telephone to determine participation eligibility using a standardized script. Asymptomatic participant inclusion criteria included:

- Age ≥50 years
- Not a candidate for total joint replacement surgery
- No cardiovascular disease (controlled high blood pressure acceptable)
- No neurological disease
- No musculoskeletal disease or injury
- No lower limb surgery within the past year
- Ability to walk independently without ambulatory aid
- Self-reported ability to:
    - Jog 5 meters
    - Walk more than a city block without aid
    - Climb stairs in a reciprocal fashion (i.e. one foot over the other)

All eligible participants were provided with a detailed description of the study procedures and expectations, a copy of the informed consent form, as well as directions to the JAR laboratory at Dalhousie University.

3.1.3 Sample Size

To our knowledge, no studies exist that test the objectives of this thesis across the three samples of knee OA, hip OA, and an asymptomatic group. Therefore, sample size was based on an estimate from a combination of literature comparing individuals with knee OA with asymptomatic populations.[23,28,29,175] Samples sizes of these studies ranged from 15 to 60. While gait analyses generally include a variety of biomechanical and electromyographical outcomes incorporating joint moments and neuromuscular activations, sagittal plane flexion-extension moments are a key feature consistently reported to differ with presence and severity of knee OA.[23,28,29,31,175] Upon reviewing

literature pertaining to sagittal plane knee moments, the difference or range from peak knee flexion moment to peak knee extension moment during stance is a frequently reported outcome[28,31,175] and has been shown to be an outcome of greater reliability than peak moment measures.[119] Rutherford and colleagues (2020) reported an ICC of 0.93 for the range from peak knee flexion moment to peak knee extension moment, whereas the ICCs for peak flexion and peak extension alone were 0.78 and 0.80, respectively.[119] Therefore, the range from peak knee flexion moment to peak knee extension moment was selected for this sample size analysis. Rutherford and colleagues (2017) reported a significant difference of 0.25Nm/kg (standard deviation (SD)=0.21Nm.kg) in the range from peak knee flexion moment to peak knee extension moment between individuals with moderate knee OA and asymptomatic older adults.[28] This difference in sagittal plane knee flexion-extension moment range is greater than the MDC reported to be 0.16Nm/kg for dual-belt treadmill gait in asymptomatic adults.[119] Furthermore, related research investigating measures of peak flexion moment during stance among individuals with knee OA have reported similar standard deviations of approximately 0.2Nm/kg.[119,131,144]

The power and sample size calculation were completed in Minitab™ V.19 using a one-way analysis of variance (ANOVA). Beta (β) was set to 80% (Power = 1- β) to calculate the sample size required to reject the null hypothesis with certainty. Based on previous literature comparing moderate knee OA and older asymptomatic groups:

Difference in range from peak knee flexion moment to peak knee extension moment: 0.25Nm/kg

Standard deviation for knee flexion/extension range: 0.21Nm/kg

One-way ANOVA
α = 0.05 Assumed standard deviation =0.21
Factors:1
Number of levels: 3

Difference	Sample Size	Target Power	Actual Power
0.25	14	0.8	0.820173

Based on these estimations, a sample size of 16 subjects in each group was selected to detect significance between the groups based on a one-way ANOVA.

3.2 Procedures

All testing procedures were completed at the JAR laboratory in the School of Physiotherapy at Dalhousie University in Halifax, NS. Upon arrival, all participants were introduced to the laboratory environment, equipment, and general procedures of the data collection. Participants were asked to provide informed written consent and any questions pertaining to the consent form were answered at this time. Participants were also asked to complete self-report questionnaires specific to their affected joint and requested to report any medication consumption for the current day. Participants diagnosed with hip OA were asked to complete the Hip Osteoarthritis Outcome Score (HOOS) which has shown high test-retest reproducibility[176] and construct validity[177] for assessing patient's opinions about their hip related problems. Participants diagnosed with knee OA were asked to complete the Knee Injury and Osteoarthritis Outcome Score (KOOS) which demonstrates adequate internal consistency, test-retest reliability, and construct validity for patients with knee conditions.[178] Both the HOOS and the KOOS consist of five separate subscales, including: pain, symptoms, functions of daily living, quality of life, and sport & recreation.

3.2.1 Participant Preparation

After completion of the questionnaires, participants were instructed to change into form-fitting apparel and remove footwear for the duration of the testing protocol. Standard anthropometric measurements including height, weight, as well as hip, waist, thigh, and shank circumferences were measured. An experienced physiotherapist then performed an assessment of affected joint range of motion using standardized procedures.[179] The same physiotherapist performed the assessment for all participants using a standard goniometer affixed with a spirit level. Hip flexion and extension were measured for the hip OA group, and knee flexion and extension for the knee OA group. Two measurements of the affected joint were obtained for both flexion and extension, and each pair of measurements was averaged. Participants were then prepped for EMG sensor placement. Standardized skin preparation and electrode placement protocols consistent with SENIAM (Surface EMG for the Non-Invasive Assessment of Muscles) guidelines were implemented.[180] The participant's skin was lightly shaved and cleaned with 70% alcohol swabs. Ag/AgCl surface electrodes (10mm diameter, 30mm inter-electrode distance, Red Dot, 3M Health Care, USA) were placed in a bipolar configuration over the VL, RF, VM, MH, LH, MG, LG (Figure 3-1). Table 3-1 describes the standardized electrode placement locations for each muscle.[180] A ground electrode was placed on the anterior tibial shaft. Manual muscle tests and palpation were used to validate electrode location to ensure signal quality, as well as make the appropriate gain adjustments. Pre-amplified (x500) lead wires were attached to the electrode pairs on each muscle group as well as the ground electrode. All electrodes and lead lines were further secured using adhesive tape to prevent movement and accidental dislodgment. EMG

signals were recorded at 2000Hz using two AMT-8^{TM} 8-channel Bortec systems (Bortec Inc, Canada) and further amplified with gains ranging from 100-5000x (Input impedance of ~10 GΩ, CMRR:115 dB at 60 Hz, Band-pass 10-1000Hz) to maximize dynamic range of the signal without reaching saturation.[28]

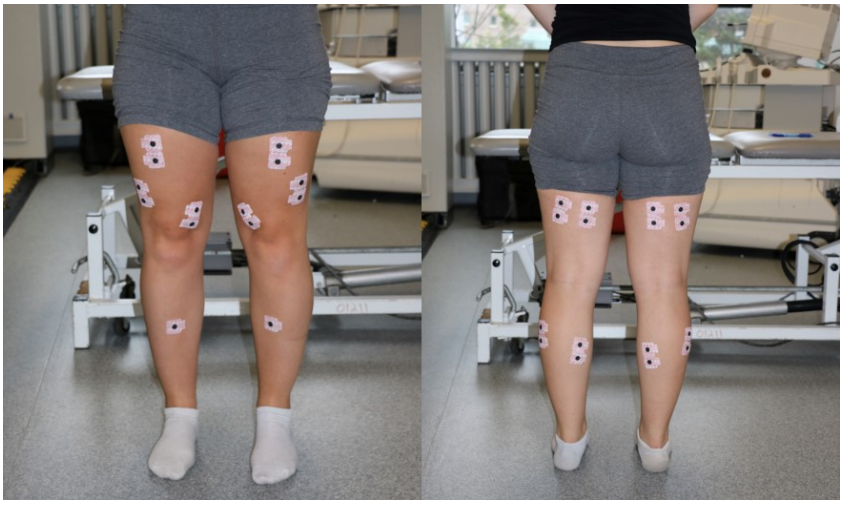


Figure 3-1. Electrode placements according to SENIAM guidelines for vastus lateralis (VL), rectus femoris (RF), vastus medialis (VM), medial (MH) and lateral (LH) hamstrings, medial (MG) and lateral (LG) gastrocnemii.

Table 3-1. Standardized electrode placement for the lower extremity according to SENIAM guidelines.

Muscle	Electrode Placement	Electrode Orientation
Vastus Lateralis (VL)	2/3 of the distance from the anterior superior iliac spine (ASIS) to lateral side of patella.	Direction of muscle fiber orientation.
Rectus Femoris (RF)	50% of the distance between the ASIS and superior patella.	Direction of lead line.
Vastus Medialis (VM)	80% of the disease from the ASIS to medial knee joint space.	Direction of muscle fiber orientation.
Medial Hamstring (MH)	50% of the distance between ischial tuberosity and medial epicondyle of tibia.	Direction of lead line.
Lateral Hamstring (LH)	50% of the distance between ischial tuberosity and lateral epicondyle of tibia.	Direction of lead line.
Medial Gastrocnemius (MG)	35% of the distance from medial knee joint space to calcaneal tubercle.	Direction of lead line.
Lateral Gastrocnemius (LG)	30% of the distance from lateral knee joint space to calcaneal tubercle.	Direction of lead line.

Upon completion of electrode placement, participants were asked to walk across a GAITRite™ portable pressure sensitive walkway approximately 10-20 times at their comfortable self-selected walking speed. Participants were verbally instructed to walk at their normal leisurely pace and the researchers did not interact with the participants during the walking trials. Five trials were randomly collected and averaged to establish the participant's appropriate self-selected speed for the instrumented treadmill.[28,175] The GAITRite™ has demonstrated excellent validity and reliability in determining gait speed in older adults.[181]

Participants were then equipped with passive, retro-reflective skin markers placed over boney anatomical landmarks including the 7th cervical vertebrae, shoulders (two finger width below the acromion processes), greater trochanters, lateral and medial femoral and tibia epicondyles, lateral and medial malleoli, head of the 1st, 2nd, and 5th metatarsals, and posterior heels, as per previously published procedures.[28] Fabrifoam® wraps were used to secure the EMG electrodes on the thigh and shanks. Clusters of four markers were then placed on rigid segments of the participant including the foot, shank, thigh, pelvis, and thoracic spine.[175,182] Both individual markers and clusters were placed bilaterally where appropriate and secured with adhesive tape. Data obtained from the upper body markers were not included in the analysis for this thesis, however, are included as part of standardized methodological procedures employed in the JAR lab and the data are being stored for later use. Participants were equipped with a torso harness to ensure safety during the walking trials.

3.2.2 Walking Protocol

Participants walked barefoot on the R-Mill (Motekforce Link, Culemborg, the Netherlands) dual-belt instrumented treadmill set to their pre-determined walking speed from the GAITRite™ walkway. Three-dimensional retro-reflective marker motion was sampled at 100Hz using eight Qualisys® OQUS 500 motion analysis cameras (Qualisys®, Gothenburg, Sweden) concurrently with EMG signals, as well as three-dimensional GRFs sampled at 2000Hz using the force plates instrumented in the treadmill.[28] All analog signals were analog-to-digital converted (16bit, +/- 5V) and synchronized using Qualisys® Track Manager V2.10.

3.2.3 Motion Capture Calibration & Virtual Markers

A 120-second calibration trial of the treadmill volume was completed prior to collection to align the coordinate system of each of the eight motion capture cameras to the coordinate system of the R-Mill treadmill. Participants then completed a standing calibration trial where they stood on the treadmill with their feet shoulder width apart and facing forward for a two second collection. After the completion of this trial, the retro-reflective markers placed on the greater trochanters, medial femoral epicondyles, medial and lateral tibial epicondyles, medial malleoli, and 1st and 5th metatarsals were removed.

Virtual point trials were then collected to define the anatomical landmarks for the sternal notch, and bilateral anterior superior iliac spines using a pre-calibrated digitizer wand. The position of all retro-reflective markers, rigid clusters, and virtual markers is illustrated in Figure 3-2.

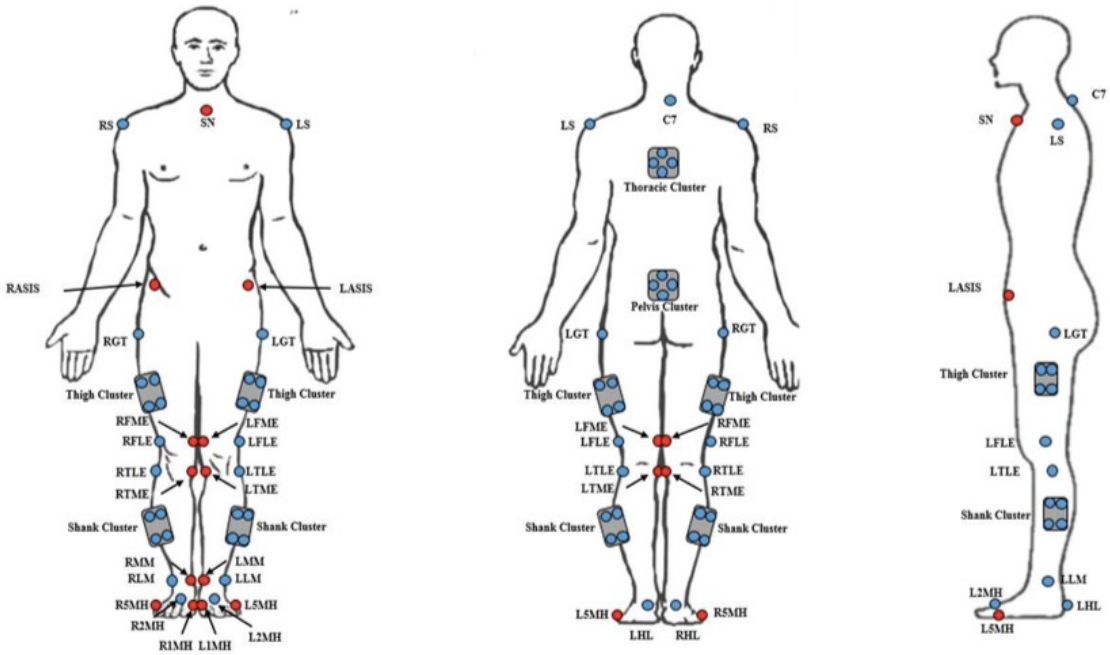


Figure 3-2. Illustration of full skin marker set placement. Clusters are indicated by grey squares with blue balls, virtual markers are represented by red balls, and individual markers placed on boney anatomical landmarks are represented by blue balls.

3.2.4 Warm-Up & Walking Trials

Prior to starting the walking trials, participants were verbally instructed to remain in the middle of the treadmill with the objective of walking with one foot on each treadmill belt. The torso harness worn by the participant was secured to the ceiling with a rope. The participants were notified when the treadmill was about to start and were encouraged to use the railings initially to become comfortable with the treadmill. Participants completed a 6-minute familiarization period, without using the railings, to acclimatize to the level of exercise, equipment, and treadmill speed.[28,52] Upon completion of the familiarization period, a 20-second collection was completed.

3.2.5 MVIC Strength Testing

After completion of the walking trials, all retro-reflective skin markers and clusters were removed from the participant. EMG electrodes and Fabrifoam® wraps remained secured for the strength testing portion of the testing protocol. Participants first completed a one-second resting subject bias trial where they were required to lay supine and asked to relax and remain as still as possible. This subject bias trial was quality checked for minimal muscle activity and followed by MVIC trials for EMG normalization purposes.

Participants performed a series of three exercises including knee flexion and extension on the Humac Norm Isokinetic dynamometer (Computer Sports Medicine Inc., USA) and unilateral standing calf raise on the floor. Two trials of each exercise were performed. Knee flexion and extension exercises were completed with the knee placed in 45º of flexion and the hip at 90º of flexion.[51] The dynamometer axis was aligned with the lateral epicondyle of the knee (axes of rotation) and the shin pad of the dynamometer arm was positioned at the distal tibia. Participants were required to isometrically push against

the shin pad (knee extension) or pull into the strap around the shin pad (knee flexion) for three seconds at maximum effort. Stabilizing straps placed on the thigh of the testing limb and around the hips to prevent movement of the upper body during testing. The unilateral standing calf raise was completed with the participant standing on the floor with no added resistance.[183] At least 40 seconds of rest separated each trial, with a minimum of 10 seconds separating each exercise. Standardized verbal encouragement was given during the trials to inspire maximal effort and consistent contractions.[51,150]

Raw voltage signals were converted to torque (Nm) measurements and gravity corrected. The Humac Norm computes the Maximum Gravity Effected Torque (MaxGET) as shown below (Eq. 3.1 & 3.2), and along with the limb position and direction of motion, adjusts the torque values for the effect of gravity on the limb. EMG data was continuously recorded during the MVIC trials and stored for later processing.

Extension Exercise (limb resisted by gravity): (3.1)

Reported Torque = Measured Torque + (MaxGET*Cosine(45º))

Flexion Exercise (limb assisted by gravity) (3.2)

Reported Torque= Measured Torque – (MaxGET*Cosine(45º))

3.3 Processing

All data was processed using pre-programmed software (JAR V. 3 & 4) written in MatLab™ 2016a (Mathworks Inc., Massachusetts, USA). Heel-strike and toe-off events were determined using a 30N vertical GRF threshold.[28]

3.3.1 Kinematics Processing

Technical and local anatomical bone embedded Cartesian coordinate systems[184] as recommended by the International Society of Biomechanics,[185] corresponding with the pelvis, thigh, shank, and foot were derived using skin markers, rigid clusters, and virtual

points. Sagittal plane knee angles will be calculated using a six-degree of freedom (DOF) model through Cardan rotations, with the order flexion/extension, abduction/adduction, and internal/external rotation, where flexion, adduction, and internal rotation of the knee are described as positive angles. The three translational DOF were ignored. In this model, joint angles are designated as the distal segment moving in regard to a fixed proximal segment.[33,67]

All motion data was smoothed using a low-pass 4th order Butterworth recursive filter with a cut-off frequency of 6Hz, and all angle waveforms were time normalized to 100% of the gait cycle, beginning at heel strike and concluding at heel-strike of the ipsilateral leg.

3.3.2 Kinetics Processing

Three-dimensional GRFs were calculated using a calibration matrix and the signal output of six sensors embedded under each of the force plates of the treadmill (Motekforce Link, Culemborg, the Netherlands) aligned with the global coordinates of the motion capture system. GRFs were low-pass filtered using a 4th order Butterworth recursive filter with cut-off frequencies of 30Hz.[186] The center of pressure (COP) was calculated using equations provided by the dual belt instrumented treadmill company (Motekforce Link, Culemborg, the Netherlands) and low-pass filtered using a 4th order Butterworth recursive filter with a cut-off frequency of 6Hz. The knee joint center (KJC) was defined based on the skin surface marker trajectories detailed above, as the mid-point between lateral and medial epicondyles.[124]

An inverse dynamics approach including GRF, kinematics, subject anthropometrics, and inertial properties was used to derive three-dimensional external

joint moments.[124] To calculate the forces and moments, free body diagrams were established for each body segment as shown in Figure 3-3. A summation of the external forces and moments acting about each segment's centre of gravity were used to calculate each segment's rate of change of linear and angular momentum.[187] Three-dimensional joint forces and moments were calculated and expressed in terms of a joint specific coordinate system.[184] Moments were normalized to body mass (Nm/kg) and time normalized to 100% of the stance phase, marked as heel strike to ipsilateral toe off.

Positive KAM angular impulse was calculated using a trapezoidal integral function where the positive area under the KAM curve over the duration of the stance phase was averaged and represented as mean KAM impulse.

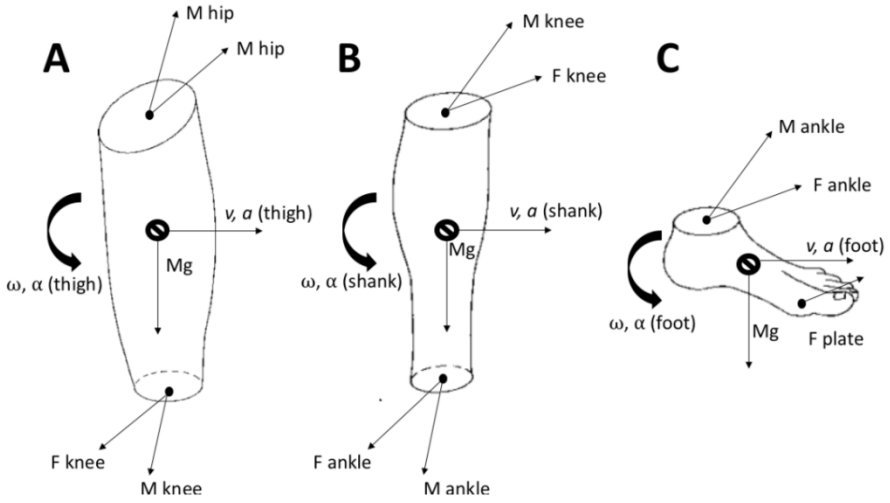


Figure 3-3. General free-body diagrams of the lower extremity segments illustrating the external moments (M) and forces (F) in the X, Y, & Z dimensions computed through segmental modeling. Linear velocity and accelerations of the segments are represented by v and a, respectively. Angular velocity and accelerations of the segment are represented by ω and α, respectively. Mg represents the mass of the segment multiplied by the acceleration of gravity and F plate represents the 3D resultant force applied onto the foot from the force plate. Adapted from Vaughan (1999)[187].

3.3. EMG Processing

All EMG signals were visually checked for dynamic range saturation, movement artifacts, or the presence of 60 Hz power-line noise. Fast Fourier transforms were completed for each participant to verify the power-spectrum of the EMG signal. After reviewing the data, signals were corrected for subject bias and gains, converted to microvolts, band-pass filtered using a 4th order Butterworth filter with cut-off frequencies of 10Hz and 500Hz, and full wave rectified. The rectified signals were filtered using a low-pass 4th order Butterworth recursive filter with a cut-off frequency of 6Hz.[28,46]

Maximum signal amplitudes for each MVIC exercise were determined using a 100-millisecond moving average window algorithm.[46] The electromyograms from the walking trials were normalized to these maximum amplitudes (%MVIC). A 500-millisecond moving average window algorithm was used to determine the maximum torque generated across the three-second MVIC contractions and the average of both exercise trials was calculated as the maximum torque generated by each participant for each muscle.[28]

3.5 Data Analysis

The limb diagnosed with OA was chosen for analysis for both the knee OA and hip OA groups, while a random leg was chosen for the asymptomatic participants. Sixteen individuals with hip OA were recruited and gait data collected specifically for this thesis. Of the 89 knee OA and 48 asymptomatic participants in the database (data collected between 2015 and 2020), the first 16 individuals of each sample who walked at a self-selected velocity of ±0.10m/s of the average walking speed of the hip OA group and who were the best matched for demographics of sex and age were selected. Discrete variable analysis has been previously used in OA literature to investigate three-

dimensional joint mechanics[24,33,150,188] and previously tested metrics were isolated from the current data.

The sagittal plane knee angle at the instance of initial contact, as well as ranges of knee motion from initial contact to peak flexion during loading response, and peak flexion to minimum flexion during terminal stance, were obtained from the sagittal plane knee motion and are outlined in Table 3-2. These metrics are displayed on Figure 3-4 for illustration purposes.

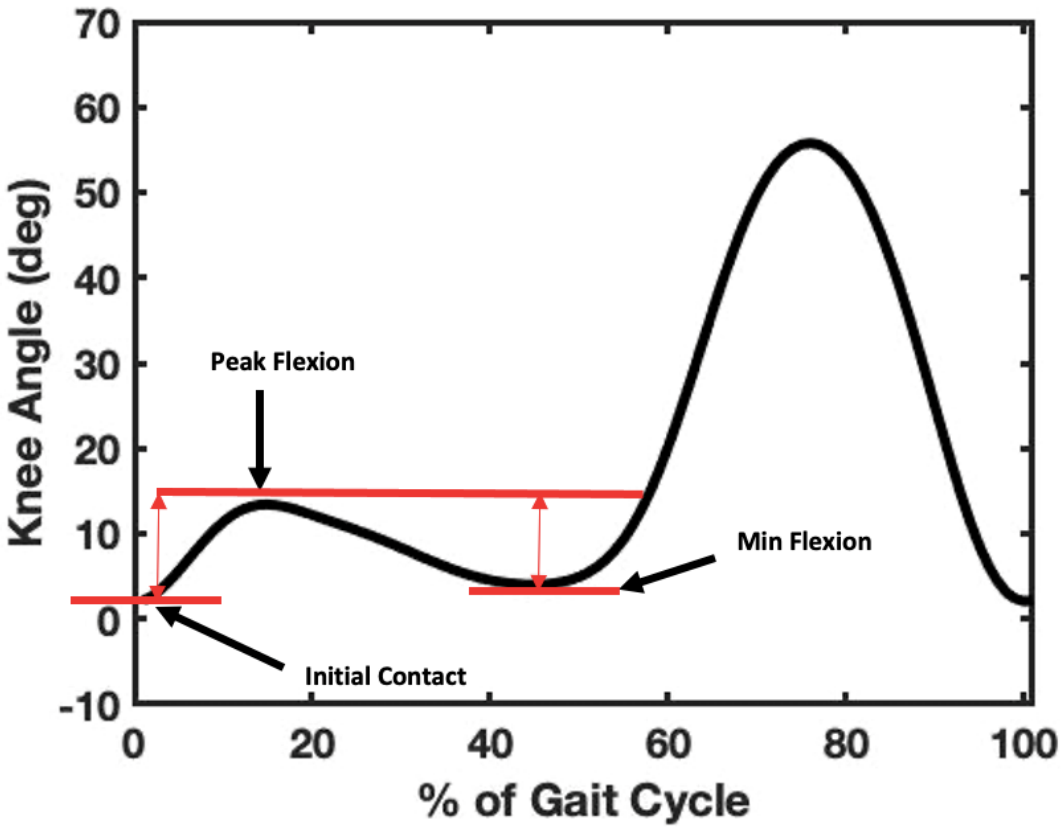


Figure 3-4. Example of sagittal plane knee joint motion in degrees throughout the gait cycle. Instances of initial contact, peak knee flexion and minimum knee flexion are outlined on the figure by the black arrows. The ranges of knee joint motion from initial contact to peak flexion during loading response, and from peak flexion to minimum flexion during terminal stance are outlined on the figure by the red arrows for illustration purposes.

Discrete metrics from the sagittal and frontal plane moments calculated through inverse dynamics analysis included the range between the peak knee flexion moment (KFM) to the peak knee extension moment (KEM), the overall peak KAM, as well as KAM impulse calculated from the non-time normalized data. All frontal and sagittal plane discrete metrics that will be analyzed are displayed in Table 3-2 and illustrated in Figures 3-5 & 3-6.

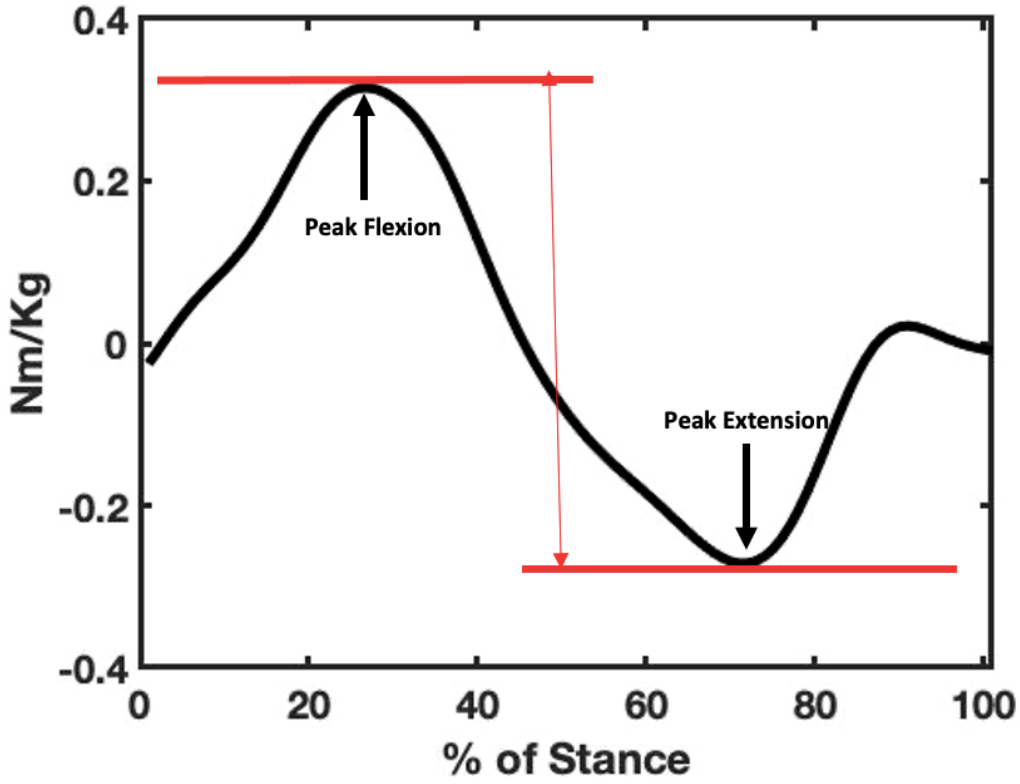


Figure 3-5. Example of sagittal plane flexion-extension moment in Nm/Kg throughout the stance phase of the gait cycle. Instances of peak knee flexion moment and peak knee extension moment are outlined on the figure by the black arrows. The ranges from peak flexion moment to peak extension moment is outlined on the figure by the red arrows for illustration purposes.

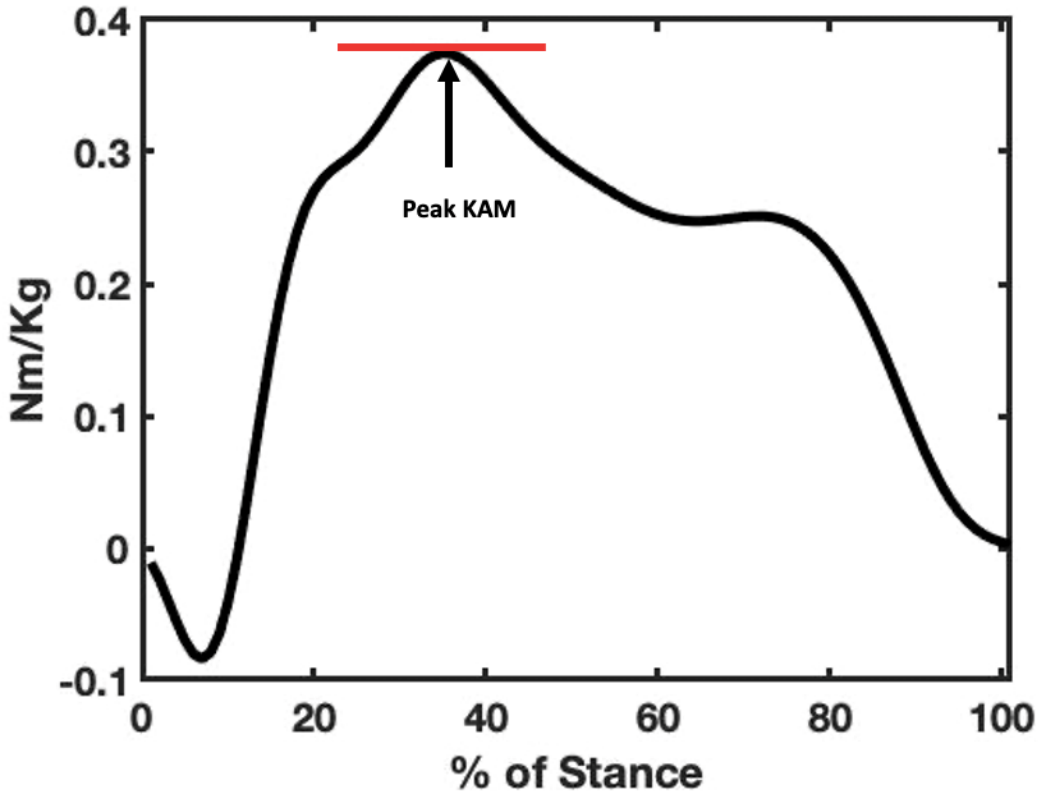


Figure 3-6. Example of frontal plane knee adduction moment (KAM) in Nm/Kg throughout the stance phase of the gait cycle. Peak KAM is outlined on the figure by the black arrow.

Mean MVIC normalized knee joint muscle activation amplitudes throughout the stance phase will be compared between participant groups for the hamstrings, quadriceps, and gastrocnemii. An example of mean MVIC normalized activation amplitude is illustrated in Figure 3-7. Lateral: medial muscle activation ratios were computed by subtracting the mean MVIC normalized *medial* muscle amplitude from the *lateral* amplitude for the quadriceps (VL:VM), hamstrings (LH:MH), and gastrocnemii (LG:MG).

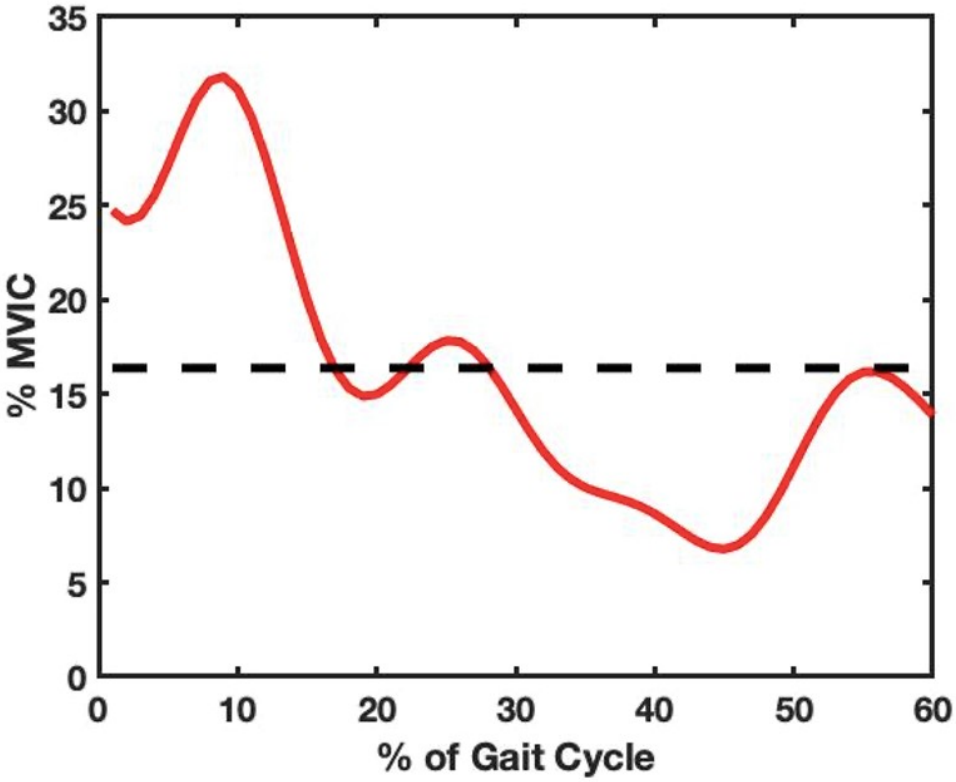


Figure 3-7. Example of mean MVIC normalized medial hamstring activation represented by the red line. The average muscle activation amplitude throughout the stance phase of the gait cycle is represented by the black dashed line.

Table 3-2. Equations used to calculate discrete metrics from sagittal plane motion & moments, frontal plane moments, and neuromuscular activations.

Discrete Metric	Description
Initial contact to peak flexion during loading response	Peak flexion during early stance (1-30% of Gait Cycle) minus flexion angle at initial contact (Degrees)
Peak flexion during loading response to minimum flexion during terminal stance	Peak flexion during early stance (1-30% of Gait Cycle) minus minimum flexion during terminal stance (30-60% of Gait Cycle) (Degrees)
Peak KFM to peak KEM	Peak extension moment (50-100% of Stance) minus peak flexion moment (15-40% of Gait Cycle) (Nm/kg)
Peak KAM	Overall maximum knee adduction moment (1-100% Stance) (Nm/kg)
KAM Impulse	Positive knee adduction moment angular impulse (Nm•s/kg)
VL:VM Ratio	Mean vastus lateralis activation amplitude (1-60% Gait cycle) minus mean vastus medialis activation amplitude (1-60% Gait cycle) (%MVIC Difference)
LH:MH Ratio	Mean lateral hamstring activation amplitude (1-60% Gait cycle) minus mean medial hamstring activation amplitude (1-60% Gait cycle) (%MVIC Difference)
LG:MG Ratio	Mean lateral gastrocnemius activation amplitude (1-60% Gait cycle) minus mean medial gastrocnemius activation amplitude (1-60% Gait cycle) (%MVIC Difference)

3.6 Statistical Analysis

Assumptions of equal variance and normality were tested using Levene's test and Kolmogorov-Smirnov, respectively, for all continuous variables ($\alpha = 0.05$). All data with unequal variances or non-normal distributions were transformed using the Johnston Transformation algorithm in Minitab^{TM} V.18. One-way ANOVAs were used to determine significant differences between the three groups for subject demographics, biomechanical metrics and lateral: medial muscular activation ratios. Bonferonni post-hoc testing was

used for all significant effects and significance was determined to be alpha (α) $\leq$ 0.05. Cohen's *d* effect size was used to compare group outcomes with the classification of nil (*d* <0.2), small (*d*=0.2-0.5), medium (*d*=0.5-0.8), and large (*d*>0.8).[189] All statistical analyses were completed in Minitab™ V.18 (Minitab Inc., Pennsylvania, USA).

Chapter 4 Results

From a database of 153 participants, including 89 with knee OA, 16 with hip OA, and 48 asymptomatic healthy adults, 16 individuals were identified in each group that satisfied the inclusion criteria and could be matched for sex, age, and walking velocity. Participant characteristics are found in Table 4-1. Groups were similar on all demographic variables except mass (p=0.01) and BMI (p=0.001), where individuals with knee OA were heavier, with greater BMI, than individuals with hip OA and asymptomatic individuals. There were no significant differences between any of the groups for age (p=0.08), knee flexion (p=0.56) and extension (p=0.65) strength, or walking velocity (p=0.45).

Table 4-1. Mean (Standard deviation) participant characteristics for the knee OA, hip OA, and asymptomatic (ASYM) groups.

Variable	Knee OA	Hip OA	ASYM
n	16	16	16
n Females	10	10	10
Age (years)	61(6)	56 (4)	61 (8)
Mass (kg)	85.1 (12.1)^{A}	76.8 (18.4)^{AB}	68.2 (11.2)^{B}
BMI (kg/m^2)	29.8 (3.80)^{A}	27.0 (4.33)^{AB}	24.7 (2.97)^{B}
Walking velocity (m/s)	1.04 (0.01)	1.04 (0.11)	1.07 (0.06)
Knee flexion strength (Nm)^	68.7 (20.1)	77.4 (27.8)	77.1 (28.4)
Knee extension strength (Nm)^	117.9 (36.3)	133.4 (53.6)	125.4 (44.5)
Radiographic grade (n)*			
KL 0	2	-	-
KL I	7	-	-
KL II	4	-	-
KL III	2	-	-
KL IV	0	-	-

For each variable, unlike letters indicate significant difference (p<0.05).
**one knee OA participant did not have a KL grade.*
^one hip OA participant did not have strength data.

Kellgren Lawrence classification of radiographic osteoarthritis severity scores for the knee OA group are outlined in Table 4-1. Most knee OA participants were classified as KL grades I and II, with only two participants classified as 0 and III, and no participants with a KL grade of IV. Self-reported measures of pain and function for the individuals with knee OA and hip OA are outlined in Table 4-2. Average passive range of motion measurements for the affected joint of the OA groups are presented in Table 4-3.

Table 4-2. Knee injury and Osteoarthritis Outcome Score (KOOS) and Hip disability and Osteoarthritis Outcome Score (HOOS) subscale scores for symptoms, pain, function in daily living (ADL), and quality of life for the knee OA and hip OA groups, respectively.

Questionnaire Score	Knee OA (KOOS)	Hip OA (HOOS)
Symptoms (x/100)	61.2 (10.8)	63.4 (15.0)
Pain (x/100)	70.8 (13.1)	63.0 (17.1)
ADL (x/100)	82.0 (10.4)	70.9 (16.1)
Quality of Life (x/100)	48.0 (18.9)	42.2 (18.8)

Interpretation: Higher score indicates less severe joint-related problems.

Table 4-3. Clinician-measured passive range of motion metrics of the knee and hip joints for the knee OA and hip OA groups, respectively.

Passive Range of Motion	Knee OA	Hip OA
Knee flexion (deg.)	132 (10.7)	-
Knee extension (deg.)	-1.25 (2.34)	-
Hip flexion (deg.)	-	103 (13.7)
Hip extension (deg.)	-	16.8 (6.62)

The mean (SD) biomechanical variables and neuromuscular activation ratios for the three groups are outlined in Table 4-3. Sagittal plane knee joint motion is shown in Figure 4-1. No significant group differences were noted in the sagittal plane knee motion ($p>0.05$). Although not significant, a large effect size ($d=0.80$) was found for the range from initial contact to peak flexion during loading response for the knee OA group in comparison to the hip OA and asymptomatic groups (3 degrees).

Table 4-3. Mean (Standard deviation) biomechanical outcomes of walking and Lateral: Medial muscle activation ratios for each group.

Variable	Knee OA	Hip OA	ASYM
Sagittal Plane Knee Biomechanics			
Initial contact to peak flexion during loading response (deg.)	11 (4)	14 (4)	14 (3)
Peak flexion during loading response to minimum flexion during terminal stance (deg.)	10 (5)	10 (6)	11 (4)
Peak KFM to Peak KEM (Nm/kg)	0.58 (0.20)	0.62 (0.20)	0.73 (0.20)
Frontal Plane Knee Biomechanics			
Peak KAM (Nm/kg)	0.39 (0.10)^{A}	0.30 (0.11)^{B}	0.38 (0.07)^{AB}
Impulse (Nm•s/kg)	0.14 (0.04)^{A}	0.09 (0.05)^{B}	0.13 (0.03)^{A}
Lateral: Medial Muscle Activation Ratios (%MVIC difference)*			
VL:VM	3.5 (6.5)	-0.2 (3.4)	1.9 (5.4)
LH:MH	4.4 (6.2)^{A}	-0.3 (2.3)^{B}	0.1 (3.7)^{B}
LG:MG	-16.8 (9.2)	-19.2 (10.8)	-17.9 (10.2)

For each variable, unlike letters indicate significant difference ($p<0.05$).
** one hip OA participant did not have electromyography data.*

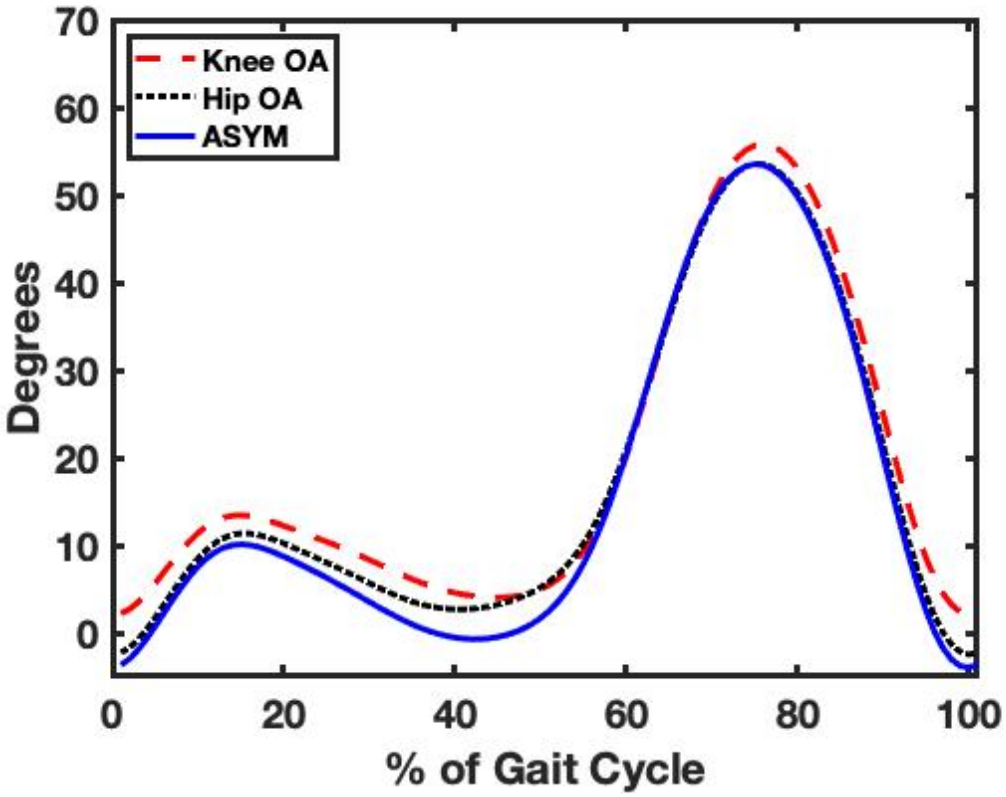


Figure 4-1. Sagittal plane knee joint kinematics for the knee OA, hip OA, and asymptomatic groups. The knee OA group is represented by the dashed red line, the hip OA group is represented by the dotted black line, and the asymptomatic (ASYM) group is represented by the solid blue line. Degrees of knee joint flexion are on the y-axis, where a positive value indicates knee flexion, and percent of gait cycle is on the x-axis.

Sagittal plane flexion-extension moment for the three groups is demonstrated in Figure 4-2. No group effects were found for the range from peak flexion to peak extension ($p<0.05$), however moderate effect sizes were found for knee OA ($d=0.75$) and hip OA ($d=0.55$) groups in comparison to the asymptomatic group (0.15Nm/kg & 0.11Nm/kg, respectively).

The frontal plane KAM for all groups is outlined in Figure 4-3. The peak KAM was greater in individuals with knee OA compared to individuals with hip OA only ($p=0.02$), whereas frontal plane impulse was greater in asymptomatic and knee OA

individuals compared to individuals with hip OA (p=0.003) and no differences were found between ASYM individuals and those with knee OA (p=0.242).

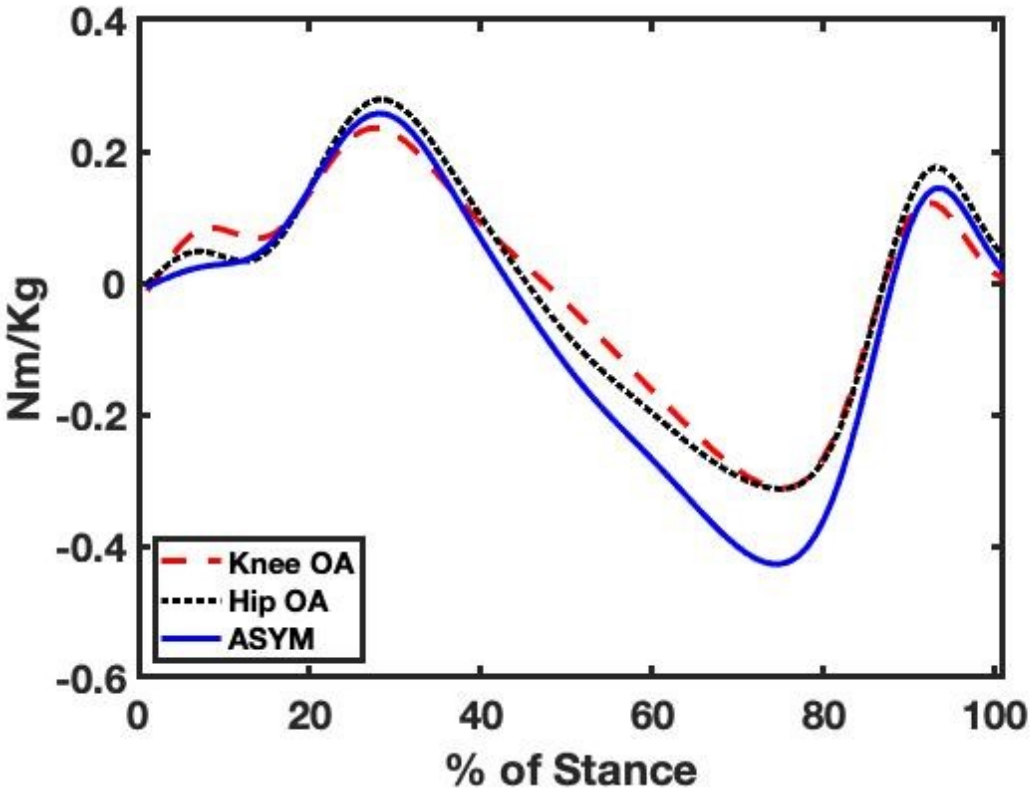


Figure 4-2. Sagittal plane knee flexion-extension moments for the knee OA, hip OA, and asymptomatic groups. The knee OA group is represented by the dashed red line, the hip OA group is represented by the dotted black line, and the asymptomatic (ASYM) group is represented by the solid blue line. A positive value indicates a net external flexion moment and a negative value indicates a net external extension moment. Percent of stance phase is on the x-axis.

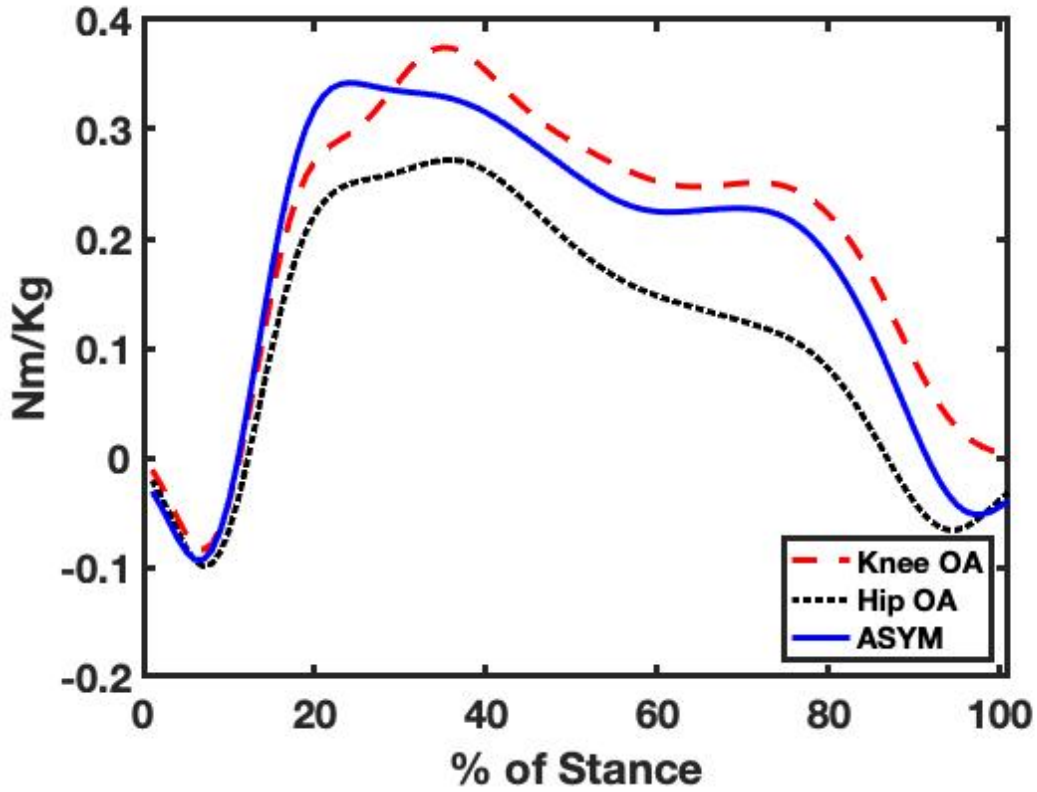


Figure 4-3. Frontal plane knee adduction moment for the knee OA, hip OA, and asymptomatic groups. The knee OA group is represented by the dashed red line, the hip OA group is represented by the dotted black line, and the asymptomatic (ASYM) group is represented by the solid blue line. A positive value indicates a net external adduction moment and a negative value indicates a net external abduction moment. Percent of stance phase is on the x-axis.

A significant group effect was found in the lateral: medial hamstring activation ratio, where individuals with knee OA had a greater lateral: medial muscle activation ratio compared to both asymptomatic and hip OA groups, meaning there was more LH activation than MH activation during the stance phase of the gait cycle. This finding is demonstrated in Figure 4-4. No other group differences in VL:VM or LG:MG activation ratios were found, as shown in Figures 4-5 and 4-6. Individual waveforms for each participant group for all gait variables studied are available in Appendix A.

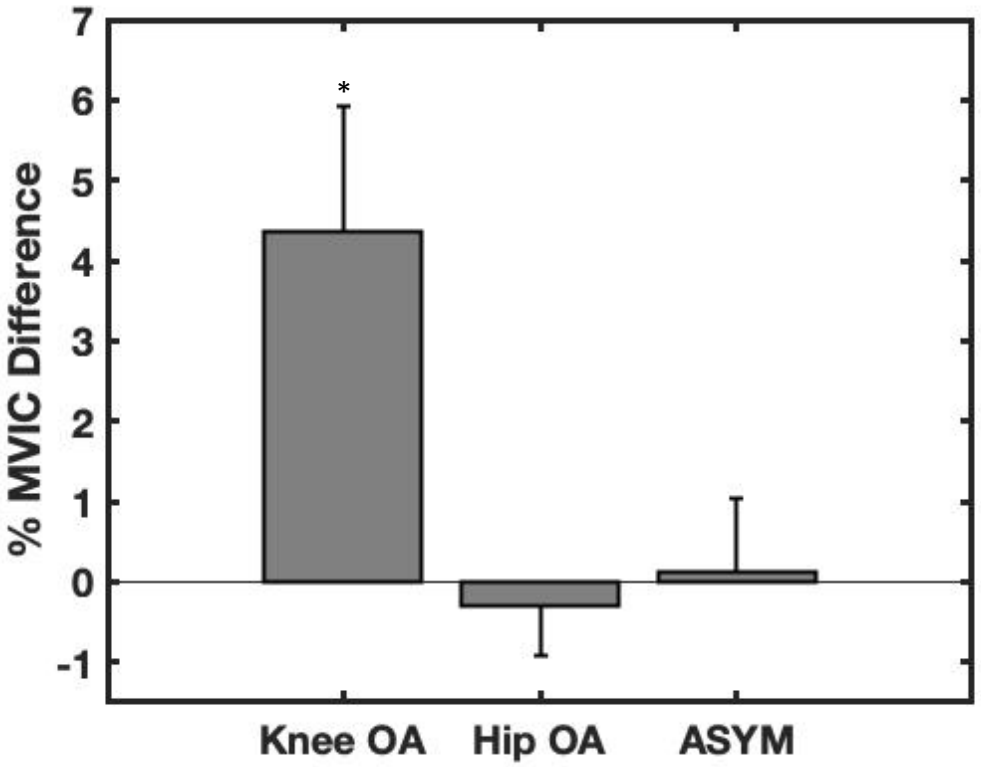


Figure 4-4. Mean lateral: medial hamstring (LH:MH) activation ratios (with error bars representing standard error (SE= SD/√n)) for the knee OA, hip OA, and asymptomatic (ASYM) groups. Significant difference compared to the other groups is denoted by a "".*

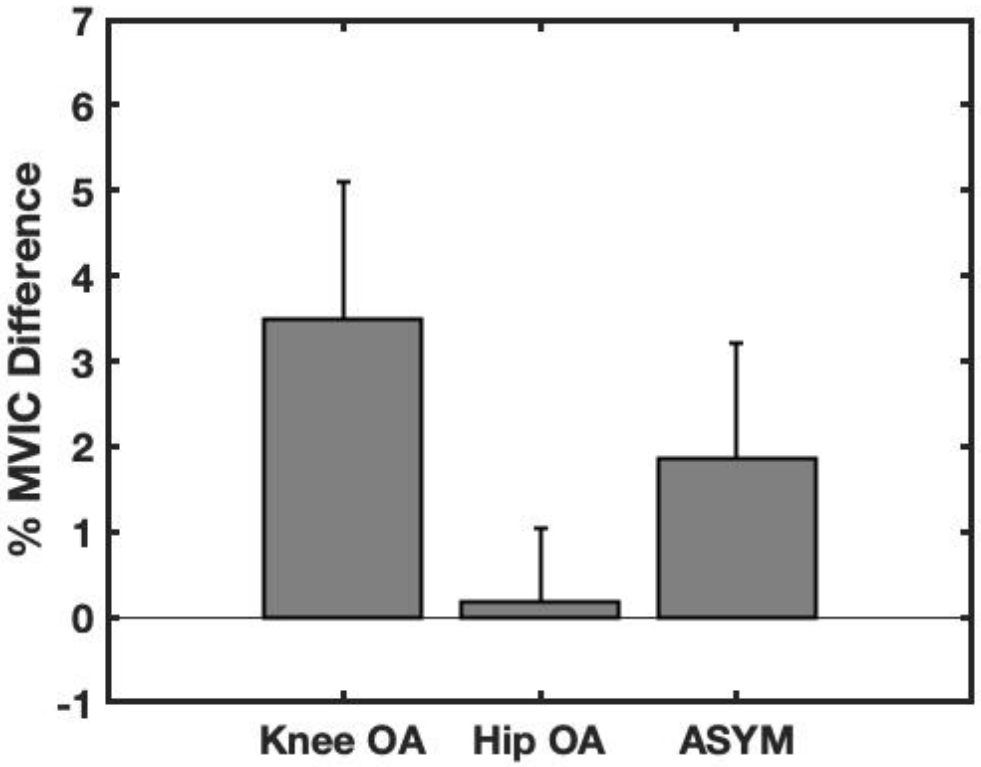


Figure 4-5. Mean vastus lateralis: medialis (VL:VM) activation ratios (with error bars representing standard error (SE= SD/√n)) for the knee OA, hip OA, and asymptomatic (ASYM) groups.

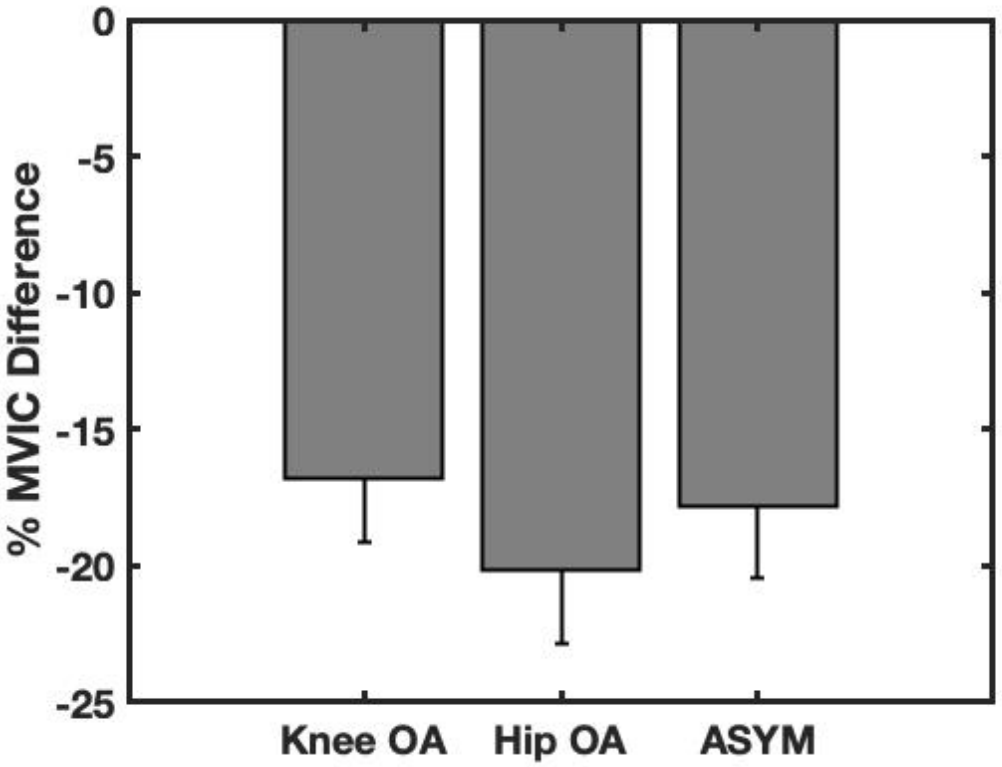


Figure 4-6. Mean lateral: medial gastrocnemii (LG:MG) activation ratios (with error bars representing standard error (SE= SD/√n)) for the knee OA, hip OA, and asymptomatic (ASYM) groups.

Chapter 5 Discussion

5.1 Opening Summary

For over a decade, researchers have demonstrated that individuals with OA of the lower extremity joints show characteristic alterations in the way they walk. For individuals with medial compartment knee OA, the most commonly reported biomechanical metrics include reductions in flexion-extension motion and moments[23–29] and increases in the frontal plane KAM.[23,28,30,42] These features are consistently identified when comparing a group of individuals with knee OA to an asymptomatic group, as well as those of different disease severities.[23,25–28] Characteristic knee joint muscle activations are also found, most notably prolonged activation and differential lateral: medial muscle activation differences.[46,49,51,53,150] While these biomechanical and neuromuscular adaptations associated with knee OA presence and progression remain rather consistent, little is known about their uniqueness to the disease. In fact, whether they represent pathomechanics distinctive of knee OA exclusively or of a lower extremity pathology in general remains unknown. To our knowledge, no study exists comparing a group of individuals with medial compartment knee OA to a group with another lower extremity pathology. The main objective of this study was to determine whether specific knee joint biomechanical and neuromuscular gait outcomes previously linked to symptomatic medial compartment knee OA severity and progression are in fact unique to those with knee OA by concurrently investigating a group of asymptomatic individuals and those with moderate hip OA, with each comparator group having no known knee OA.

5.2 Sample Characteristics

To test the specific objectives, three groups of individuals were studied who were matched on age, sex, and walking velocity. For individuals with knee and hip OA, they were matched on OA severity.

Age is an important consideration when understanding biomechanical and neuromuscular gait outcomes. As we age, changes occur to our passive, active and neurological systems that can impact walking. These may include alterations to sensation, muscle strength, joint range of motion[190,191] and as such it was important to maintain a minimal age difference between study samples in the current investigation. As shown in Table 4-1, the mean age of the knee OA participants in this study was 61 years, the hip OA participants was 56 years, and the asymptomatic group was 61 years. Age ranges from 51-64 years have been previously described in study groups with moderate severity knee OA[28,33,46,134] and hip OA.[35,39,66] In knee OA samples, this aligns with Losina and colleagues in 2013, who estimated incidence of diagnosed symptomatic knee OA was highest among adults aged 55 to 64 years.[192] The average study group ages described in the current study surpass the clinical criterion of age>50 for diagnosis of hip and knee OA according to the ACR,[70] as well as the minimum age of 40 years described as part of the typical presentation of peripheral joint OA in the EULAR recommendations for clinical management.[12] Together, participant age in the current study is within a range where OA can be present and impact function in some people. The similar age among participants also helps negate the impact of age on gait speed.

As walking speed generally declines with age[193] and progression of OA,[194] determining what gait changes are associated with the disease process, and those that are

the result of differences in gait speeds poses a challenge for researchers. All three participant groups were matched for walking velocity, as shown in Table 4-1. Previous literature has reported an average self-selected walking speed range of 0.9-1.4m/s for individuals with moderate severity medial knee OA during dual belt treadmill walking.[28,134] Similarly, Constantinou and associates (2014) in their systematic review on spatial-temporal characteristics in individuals with hip OA reported the average self-selected speed was 0.95 (0.19) m/s.[195] The group-matched walking velocity established in the current study is comparable to previously reported gait velocities for individuals with knee and hip OA. However, the comparison between gait speeds of OA groups and asymptomatic controls seems to be more variable. Several studies have shown individuals with moderate knee OA walk slower than controls,[28,32,175] while others report comparable speeds.[23,33,42,134]

It is widely recognized in the literature that differences in walking speeds can cause difficulties with the interpretation of gait analysis results such as joint motion, moments, and neuromuscular activations.[42,51,134,194,196] Several approaches have been used to account for walking velocity, including having participants walk at pre-determined speeds,[24,52,196,197] statistically controlling for the variable by entering it as a covariate during analysis,[32,35,133,134] or rather just describing the velocity as self-selected and reporting the group differences.[37,47,67] All three approaches have limitations when attempting to differentiate the effect of walking velocity that occurs with progression of the disease from changes associated with structural and symptomatic differences resulting in biomechanical changes of the joints.[51] Another strategy is to control for velocity in the analysis phase of the study protocol by selecting and comparing subgroups of each

population based upon their self-selected walking speed. This method was chosen for the current study based upon previous methods by Rutherford and colleagues (2011) where three groups of participants including asymptomatic, moderate knee OA, and severe knee OA were matched for walking velocity. Results of the study demonstrated that individuals with varying clinical presentations of knee OA who chose to walk at similar velocities, still presented with characteristic neuromuscular alterations.[51] These findings support the use of matching walking velocities among groups of varying OA presentations. A limitation of this method is that the groups may not reflect the general populations of individuals with and without OA. While the velocity selected for this study was in fact the average speed for the entire hip OA sample of 16 subjects and is a comparable self-selected speed for OA populations based upon previous publications, it may not be a true representation of the typical walking speed for healthy community-dwelling older adults which has been reported to be up to 1.30m/s.[198] Caution should be taken in extrapolating these findings to the knee and hip OA populations as a whole.

The study groups were also matched for sex, as few studies have differentiated biomechanical features between males and females in both knee[199–201] and hip[202] OA gait. The potential confounding effect of sex is minimized in the current study by including equal distributions of males and females in each group. The higher number of female participants included in the current study is reflective of the population demographics of knee OA, where incidence rates are higher in females compared to males.[203]

Knee and hip OA participants in the current study were determined to be of moderate disease severity based upon ineligibility for total joint replacement at the time of the data collection, as well as ability to meet functional criterion outlined by Hubley-

Kozey and colleagues (2006).[46] While direct statistical comparisons could not be made, the self-report measures of pain and function for the knee and hip OA groups as measured by the standardized outcome measures KOOS and HOOS, respectively, were similar between groups across the four domains of symptoms, pain, ADLs, and quality of life (Table 4-1). With regard to radiographic severity, most knee OA participants were classified as KL grades I and II, with only two participants classified as 0 and III, and no participants with a KL grade of IV. Radiographic scores for the hip OA group were not collected and therefore not included in the current study. However, given the lack of need for diagnostic imaging in patients presenting with typical symptoms[12] and the poor correlation to functional outcomes[204–207] it is not likely to change the interpretation of the findings. Passive range of motion measures indicate the knee OA group was limited in knee extension, but not flexion in comparison to normative values for healthy adults aged 45-69.[208] The finding of knee extension limitations in the knee OA group coincides with previous work.[209] Measures of passive hip flexion and extension for the hip OA group were similar to results published by Baker and associates (2016) for their moderate hip OA group in their study focused on the relationship between passive hip range of motion measurements and dynamic motion during gait in individuals with different disease severities.[159] These findings further support the moderate disease severity description of the participants included in the present study.

The sample of knee OA participants included in the present study are characteristic of patients that may present to primarily health care providers with suspected or undiagnosed OA of the knee. Clinical features of older age, female gender, being overweight, restricted range of motion, and complaints of pain and/or functional

limitation are all key characteristics of OA and can help lead to a confident clinical diagnosis.[71] The participants of this study are described as a moderate disease severity based upon their functional ability, as well as their clinical characteristics of range of motion, strength, and self-report measures in comparison to previously described cohorts. These participants represent the large portion of individuals with knee OA who would benefit from first-line treatment techniques including education, exercise therapy, and weight loss advice,[11,210,211] as many would not yet be eligible for surgical interventions. Individuals with OA often do not seek help until the symptoms of their disease surpass their own self-management strategies,[212] which may indicate progression beyond mild stages of the disease by the time they seek medical intervention. Investigations into the biomechanical features of individuals representative of those likely to present to physiotherapists and physicians is crucial to continue the evolution of effective management and treatment strategies.

5.3 Objective 1

The first objective of this study was to determine if knee joint sagittal plane movement dynamics (range from peak flexion to peak extension moments, and ranges of motion through loading response and mid-to-late stance) in individuals with symptomatic unilateral medial compartment knee OA are different from the ipsilateral knee of individuals with symptomatic unilateral moderate hip OA, and asymptomatic individuals. It was hypothesized that sagittal plane dynamics would be reduced in individuals with knee OA in comparison to the hip OA and asymptomatic groups, and that there would be no differences between the hip OA and asymptomatic groups. Results of the present study partially support this hypothesis.

Movement patterns throughout the stance phase were similar for all three participant groups. Although not statistically significant, a large effect size was found for the 3-degree difference in range of motion between initial contact to peak flexion during loading response for the individuals with knee OA in comparison to both the asymptomatic knees and the ipsilateral knees of the hip OA group, which borders the previously established MDC for this gait feature.[119] As demonstrated in Figure 4-1, this difference is likely due to the increased knee flexion at the time of initial contact in individuals with knee OA in comparison to the other two groups. This finding aligns with previous studies reporting those with knee OA strike the ground in a more flexed position.[24,25,27,30] As the knees of individuals with OA transitioned from loading response to terminal stance, both the hip OA and knee OA groups show less movement towards full extension. This is present in Figure 4-2, where both the knee OA and hip OA groups demonstrate reduced extension moments during the latter phase of stance. The differences between the three groups presented in Table 4-3 are below the previously reported MDC for healthy individuals (0.16Nm/kg) supporting the statistical finding of the current results,[119] however moderate effect sizes were found for the range from peak knee flexion moment to peak knee extension moment for both OA groups. For individuals with knee OA, this less dynamic range has been previously described in comparison to healthy older adults[28,31] and is suggested to coincide with what has been described as “stiff knee” gait.[29,31,132] This less dynamic movement pattern is thought to be an adaptive strategy to overcome knee joint instability through elevated agonist and antagonist muscular activation.[23,24,29,133,134]

The lack of statistical difference for sagittal plane metrics between moderate knee OA and asymptomatic groups in the present study may be the result of matched walking velocities. Landry and colleagues (2007) demonstrated the dynamic range of the knee flexion-extension moment increases with increasing walking speed in both knee OA and control groups, primarily due to the influence on the peak knee flexion moment.[33] As all three groups had similar walking velocities in the present study, it is likely the difference in the dynamic ranges were diminished. Furthermore, the reduction in sagittal plane movement dynamics appears to become more pronounced with increasing knee OA severity. Lewek and colleagues (2006) found significant differences in knee flexion excursion during weight acceptance between individuals with knee OA who were scheduled for surgical intervention and healthy controls matched for age, sex, and walking velocity.[108] Comparably, even after Zeni et al., (2009) statistically controlled for walking velocity, the severe OA group (KL grade IV) demonstrated deficits in knee joint excursion in comparison to controls.[134] These results suggest sagittal plane knee joint dynamics are related to both knee OA severity and walking speed, both of which are likely responsible for the lack of significant differences presented in the current study.

The ipsilateral knees of individuals with moderate hip OA showed similar early stance phase movement dynamics to age, sex, and velocity matched controls. This finding was not surprising, as the individuals with hip OA included in the present study had no known knee pathologies, so it was hypothesized their knee mechanics would be similar to the asymptomatic controls. However, as the hip OA individuals transitioned from loading response to terminal stance, they began to demonstrate similar joint dynamics as the participants with diagnosed knee OA. This trend is supported by previous work by

Rutherford and colleagues (2015) who conducted a study on individuals with moderate severity hip OA (not THA candidates) comparing knee joint mechanics to an age-matched asymptomatic population and demonstrated a 5-degree reduction in range from peak flexion to peak extension during stance phase in individuals with hip OA.[66] Comparably, Eitzen and associates (2012) found that individuals with hip OA reporting mid-to-moderate symptoms showed a reduction in ipsilateral knee joint extension during the latter 50% of stance phase, where 4-to-9-degree differences were reported in comparison to controls.[39] Together these results demonstrate that as the knees of individuals with moderate hip OA transition from early to terminal stance, joint range of motion, sagittal plane moments or a combination of both may be reduced. While these outcomes were not significant in this study, effect sizes suggest that differences may be meaningful and further work is required with greater sample sizes to understand the role lower limb OA plays more fully in altering sagittal plan knee dynamics.

While there were statistically similar trends in knee joint movement dynamics demonstrated between the two OA groups, the reason behind this presentation may be different. It is important to consider the relationship between joints in the lower extremity, and how limitations in one may alter the presentation in others.[38] Osteoarthritis in the hip joint has shown to cause reduced hip extension during the late stance phase of gait in comparison to healthy controls.[35,37–39,66] Some authors suggest this reduction in hip joint extension concomitantly results in a similar limitation in the knee joint,[39,66] thereby causing the ipsilateral knee of individuals with hip OA to present with the "stiff knee" pattern that has been related to knee OA presence and progression.[29,31,132] Ornetti and colleagues (2011) investigated kinematic gait adaptations of all lower extremity joints in

a group of hip OA patients with no other lower extremity disorders. Authors reported ipsilateral knee flexion and extension angles during gait were not statistically different among individuals with hip OA and healthy controls matched for walking velocity despite the hip OA participants showing a reduction in hip extension, although trends in the data suggest a reduction in both knee flexion and extension were present.[38] Furthermore, this study did not look at the dynamic ranges of motion, rather just the absolute maximum flexion and extension angles which have shown to be less reliable.[119]

Interestingly, the interaction between hip joint motion and other lower extremity joint dynamics in the sagittal plane has not been the focus of many studies.[38,39] Eitzen and colleagues (2012) are one of the few publications to include sagittal plane knee joint moments in their analysis of hip OA gait mechanics. Similar to the present study, no significant differences were reported between mild-to-moderate hip OA and asymptomatic groups for moments in the sagittal plane. However, in observation of their flexion-extension moment waveforms, similar reductions in dynamic movement throughout the range from peak flexion to peak extension in individuals with hip OA were demonstrated as in the current study.[39] These subtle changes require further investigation as kinematic outcomes have limited ability to provide information regarding what may be occurring inside the knee joint. It is evident that information on sagittal plane knee moments in hip OA populations is limited, and future work on the impact of kinematic changes of the hip joint on lower limb joint loads and the implications for OA disease presence and progression are indicated.

When groups of individuals with similar disease severity of knee OA and hip OA are matched for age, sex, and walking velocity, and compared to asymptomatic controls,

statistically and clinically significant differences do not exist in sagittal plane movement dynamics. Given those with hip OA and asymptomatic individuals had no known knee joint injuries or disease at the time of testing, results suggest the uniqueness of sagittal plane biomechanics previously reported in knee OA literature may not be a defining feature of knee OA, or only a direct result of knee OA processes.

5.4 Objective 2

The second objective of this study was to determine if the peak KAM and KAM impulse in individuals with symptomatic unilateral medial compartment knee OA are different from the ipsilateral knee of individuals with symptomatic unilateral moderate hip OA, and asymptomatic individuals. It was hypothesized the knee OA group would demonstrate heightened peak KAM and KAM impulse measures in comparison to both the hip OA and asymptomatic groups, and that there would be no differences between hip OA and asymptomatic groups. Study findings partially supported this hypothesis.

The KAM has been one of the most widely studied gait features in knee OA literature as it thought to represent the magnitude of intrinsic compressive load distribution between the lateral and medial tibiofemoral knee compartments.[30,34,41] It has been studied in the context of a possible risk factor for OA disease development,[45] a defining feature compared to healthy individuals,[28,30,42] and linked to disease progression.[31,43–45,213]

Compared to people with hip OA, the knee OA group walked with greater peak KAM and KAM impulse, although these features were not statistically different from the asymptomatic group. These findings contrast previous studies that have reported increased KAM measures in comparison to asymptomatic controls.[28,30,42] Baliunas and

colleagues (2002) reported heightened peak KAM in individuals with radiographic evidence of medial knee OA who were being managed by conservative medical therapy, in comparison to age, and sex distribution matched asymptomatic controls during similar walking speeds.[30] In contrast, Kaufman et al (2001) reported no significant differences in peak KAM between normal subjects and patients with knee OA, however this could be attributed to the faster walking speed in the asymptomatic group.[32] Favre and others (2016) investigated the effects of modifying gait variables such as walking speed, trunk sway, step width, and foot progression angle on the peak KAM and KAM impulse of healthy individuals. Authors reported "slow" self-selected walking speeds were associated with reduced first peak of the KAM, while "fast" self-selected walking speeds reduced the KAM impulse.[214] These findings align with previous work by Robbins and Maly (2009) who reported a trade-off between an increase in duration of the medial compartment loading and decrease in total amplitude of the loading at slower gait speeds.[139] Collectively, these studies reiterate that measures of external joint moments are sensitive to changes in walking velocity.

Individuals with knee OA have shown to present with declining walking velocity and increasing stance duration throughout the progression of the disease.[23,129,215] Therefore, it is not surprising that previous work has associated KAM impulse with increasing disease severity. Thorp and colleagues (2006) reported KAM impulse was significantly higher in those with moderate radiographic knee OA (KL grade III) compared to those with mild changes (KL grade II) while peak KAM values were similar.[140] In accordance, Kean and associates (2012) suggested KAM impulse was better able to distinguish between KL grades and severity of malalignment in individuals with

knee OA compared to the peak KAM.[138] The lack of differences in frontal plane mechanics between the knee OA and asymptomatic groups in the present study is likely due to the matched walking velocities among groups, as well as the less severe disease state of the included subjects with knee OA. In contrast to Baliunas et al. (2002),[30] the knee OA participants included in the present study were primarily of KL grades I and II, whereas most of the knee OA participants included in that study were classified as KL grade III. It is possible the KAM features linked to OA disease progression are not yet pronounced in the current study sample of knee OA participants, or, as previously found, the asymptomatic controls may in fact have radiographical evidence of OA.[216]

While no differences were identified between the knee OA and asymptomatic groups, the ipsilateral knees of individuals with hip OA demonstrated significantly decreased peak KAM in comparison to the knee OA group, and reduced KAM impulse in comparison to both the knee OA and asymptomatic groups. In the work by Favre and colleagues (2016) on the relationship between gait modifications and KAM measures in healthy adults, they demonstrated that increasing trunk sway, as defined as the maximum angle between the axis from the pelvis origin to the centre of the manubrium markers, and the axis perpendicular to the walkway, had a diminishing effect on the peak KAM and KAM impulse during gait.[214] This gait adaptation has been previously described in individuals with unilateral hip OA in comparison to asymptomatic controls,[37,217,218] as it has implications for altering joint loads at both the knees and the hips.

Moreside and associates (2018) conducted a study focused on the combined effect of kinematic and neuromuscular adaptations of the trunk in individuals with moderate (non-THA candidates) and severe (THA candidates) hip OA in comparison to an

asymptomatic healthy group. Individuals with severe hip OA demonstrated ipsilateral trunk lean during early stance phase that was four times greater than asymptomatic controls.[217] By moving the centre of mass laterally over the affected hip joint, it reduces the external hip adduction moment, resulting in less force production required by the hip abductor muscles to maintain a steady pelvis, and therefore reduces compressive forces within the joint.[37,217] Bolink and collaborators (2015) are one of the few other studies who compared individuals with knee OA, hip OA, and an asymptomatic group in their analysis of frontal plane pelvis motion during gait measured using a single inertial sensor. Individuals with end-stage hip OA demonstrated significant asymmetry in pelvic motion in comparison to both the end-stage knee OA and asymptomatic groups.[218] While this adaptation is primarily reported in individuals of advanced hip OA,[37,217,218] Watelain and colleagues (2001) studied compensatory actions in subjects of early-stage OA as defined by a combination of KL grade (< III), not currently candidates for hip surgery, and functionally independent without gait aids. Authors reported a similar increase in pelvic obliquity, corresponding to a Trendelenburg sign, was utilized in the OA group to minimize the load on their painful hip, even at this early stage of disease.[219] It is possible the moderate hip OA group in the current study were implementing similar strategies to offload the affected hip, thereby simultaneously changing the dynamic loading environment of the ipsilateral knee.

While sagittal plane movement dynamics were similar between all three groups, the frontal plane mechanics of the ipsilateral knees of individuals with hip OA were altered in comparison to both the knee OA and asymptomatic groups. This may be related to gait adaptations of the pelvis and trunk in attempt to reduce loading on the affected

joint, subsequently resulting in a decrease in medial compartment knee loads. As kinematics of the trunk was not part of the present thesis objectives, it was not included in the analysis. Conversely, the KAM of the knee OA group was not different from the asymptomatic group, which may be attributed to the low disease severity of the patients of the current sample as well as the impact of matched walking velocities among groups.

5.5 Objective 3

The third objective of the study was to determine if the difference in medial and lateral quadriceps, hamstring, and gastrocnemius activation levels in individuals with symptomatic unilateral medial compartment knee OA were different from the ipsilateral knee of individuals with symptomatic unilateral moderate hip OA, and asymptomatic individuals. It was hypothesized there would be a higher LH:MH activation ratio in the knee OA group compared to the hip OA and asymptomatic groups. Additionally, that there would be no differences between hip OA and asymptomatic groups, nor any between-group differences for VL:VM nor LG:MG activation ratios. Study findings support this hypothesis.

Although OA is often thought of as an impairment that affects joint structure, passive components are only one of the key elements required to fully understand the control systems working to preserve joint function. The passive ligamentous, neural, and active musculotendinous subsystems are operating to establish a balance between joint stability and mobility.[145] Determining how neuromuscular activations differ between individuals with and without comprised knee joint function may help achieve a better understanding of the altered mechanical environment present in OA joints.[46] Electromyographical outcomes were included in this study as previously, individuals with

medial compartment knee OA have shown to differentially activate the lateral musculature of the thigh.[23,28,46,47,49,51,53,150] In contrast, when studying healthy adults without OA,[28,46,53] the contralateral knee of knee OA patients,[53,58] and younger adults with or without hip injuries,[59] these differential activations have not been found.

Increased overall LH amplitudes are the most consistently reported neuromuscular adaptation reported in individuals with medial compartment knee OA compared to asymptomatic individuals,[28,46,47,51] and has shown to progressively increase in amplitude with increasing knee OA severity.[23,47,150] In the current study, LH:MH activation ratios were higher for the knee OA group in comparison to both the hip OA and asymptomatic groups. This finding aligns with previous work by Lynn and associates (2008) who computed a medial: lateral hamstring % MVIC activation ratio by averaging EMG activation across the entire stance phase for both muscles then dividing the medial activation level by the lateral.[49] Comparably, Rutherford and Baker (2019) used raw medial and lateral RMS amplitudes over the entire gait cycle and subtracted the medial activation value from the lateral.[53] Results of both studies revealed a bias towards greater LH activity.

These findings demonstrate that differential activations of the hamstring muscles occur with the presence of knee OA despite the similarities in sagittal plane movement dynamics among all three participant groups, which may indirectly suggest that differential activation is not related to these outcomes. While not statistically significant, the 3-degree reduction in knee angle from initial contact to peak flexion during loading response was the only sagittal plane feature unique to knee OA gait, however, whether it relates to differential hamstring activation is yet to be determined.

In comparison to the knee OA and asymptomatic groups, individuals with hip OA demonstrated a negative LH:MH ratio, thereby suggesting greater MH over LH activation. Few studies exist to understand the impact of hip pathologies on knee muscle activation, and how it pertains to the uniqueness of knee OA biomechanics and surrounding muscle EMG.[66,67] In a recent paper published on young adults with FAI compared to healthy, asymptomatic controls, individuals with pathology of the hip demonstrated MH values greater than LH, where this effect was not found in the controls.[59] While the mechanism behind this preferential medial activation is difficult to speculate, previous work has suggested that individuals with FAI may adopt an internally rotated hip position during gait in an attempt to stabilize the affected joint,[59] a gait adaptation that has shown to increase medial activation levels greater than lateral when utilized by individuals with knee OA.[220] In contrary to these findings, Rutherford and colleagues (2015) used PCA to identify significant principal neuromuscular patterns between asymptomatic and moderate hip OA groups and reported a muscle main effect where MH levels of activity were greater than LH across the stance phase, however no between group differences were identified.[66] While the difference in LH:MH ratios between the hip OA and asymptomatic groups in the present study are not statistically significant, they trend towards a preferential MH>LH activation pattern for those with hip OA, and a LH≥MH activation pattern for the asymptomatic group. Furthermore, as the Rutherford et al. (2015) study normalized EMG amplitudes to the peak amplitude obtained during the gait cycle, absolute amplitude comparisons between groups could not be made, and limits the ability to compare results to the present study.

Differential activation of the quadriceps was comparable among all three groups. Both knee OA and asymptomatic groups trended towards greater VL>VM activation, with the hip OA group inclined towards greater VM>VL activation. The knee OA group had the greatest ratio biasing VL> VM, which aligns with previous work on individuals with moderate severity knee OA by Hubley-Kozey and colleagues (2006) where a higher VL recruitment for the OA group compared to controls, and similar VM recruitment amplitudes between asymptomatic and OA groups were found using PCA.[46] Quadriceps activation ratios were more similar between the hip OA and asymptomatic groups in comparison to the knee OA group, however the hip OA group trended towards VM>VL rather than the asymptomatic group ratio demonstrating VL>VM. Interestingly, Rutherford et al. (2015) identified muscle main effects for the quadriceps, where VM had a pattern of elevated activity during late stance opposed to early stance, in comparison to VL, although this was present in both the OA and asymptomatic groups.[66]

The differential activation of the quadriceps and hamstrings in individuals with knee OA has been suggested to be a learned motor pattern in attempt to decreased medial joint loading and associated disease symptoms.[25,46] Aligning with this theory, it is possible the medial>lateral hamstring and quadricep activation preferences for those with hip OA may be related to the previously mentioned medial-to-lateral shift in joint contact forces in the ipsilateral knee when a lateral trunk lean is employed during stance phase. Previous work on knee OA has associated increased overall amplitudes in muscles that produce counteracting force vectors to the increased compartmental load,[46] and therefore the medial muscles may be acting to unload the lateral compartment. However, it would then be suspected that the hip OA group would present with a knee abduction moment,

rather than a KAM. While not the focus of this thesis, previous work has associated differential activation patterns with deviations in frontal plane alignment in individuals with knee OA.[54–57] For example, Lewek and colleagues (2004) demonstrated individuals with knee OA who presented with varus alignment had localized medial knee joint laxity which was accompanied by greater medial muscle (VM-MG) co-contraction. While seemingly counter-intuitive in regard to the KAM theory, this differential activation was speculated to be an attempt to stabilize the knee joint during gait.[133] This research suggests the relationship between differential activation and knee joint loads is more complex than described by the KAM alone. Additional investigation into how features such as static and dynamic alignment, instability, and muscle activation patterns affects knee mechanics in individuals with hip and knee OA may provide insight into the evolution of lower extremity OA and relationships between knee and hip OA pathomechanics.

Gastrocnemii muscle activation ratios were statistically similar across all three participant groups, with knee OA, hip OA, and asymptomatic individuals demonstrating elevated MG activity in comparison to LG. The lack of deviation between the knee OA and asymptomatic groups corroborates the results of Rutherford and associates (2013) where no differences in overall amplitudes of gastrocnemius activation were reported between individuals with moderate knee OA (non TKA candidates) and healthy older adults, and demonstrated generally higher amplitudes for the MG compared to the LG in both groups.[150] Few studies have investigated the effect of hip OA on gastrocnemii muscle activation. Schmidt and colleagues (2016) examined muscular adaptations in individuals one day prior to their scheduled THR and described that medial

gastrocnemius activity was more plateau-like throughout the stance phase of the affected limb in comparison to healthy controls, whose activation pattern demonstrated the typical peak in terminal stance phase. However, study objectives were focused on limb asymmetries, and direct group comparisons were not made. Furthermore, lateral gastrocnemius data was not collected, making it impossible to interpret these findings in the context of the current study.[167]

In summary, hamstring activation is affected by hip OA in a direction opposite to the effect of knee OA, showing that difference in LH:MH is greatest for knee OA compared to hip OA and ASYM groups. This suggests that this differential activation, unlike sagittal plane motion, moments, and KAM, provide a gait outcome that is unique in the knee OA group compared to both hip OA and asymptomatic groups.

5.6 Limitations

Several limitations exist in this study. Firstly, differences in BMI existed between the groups. Individuals with knee OA had higher BMI values than individuals with hip OA, and the asymptomatic controls. Previous studies have shown BMI to affect knee moments in individuals with and without moderate knee OA,[221] however results of the current study demonstrated statistically similar sagittal and frontal plane moments between the knee OA and asymptomatic groups which were the two groups with the greatest BMI difference. It is also not clear how BMI may affect neuromuscular activations during walking. Secondly, although matching for walking velocity limits the effect of this confounding variable on the results, it is possible that the group matched walking velocity may not be an accurate representation of all three populations.[194] It is possible that either high functioning OA and/or low functioning asymptomatic cohorts

were captured, and therefore extrapolating these findings to the knee and hip OA populations should be done with caution. Thirdly, radiographs of the hip and knee joints were not available for the hip OA and asymptomatic participants at the time of writing this thesis. While both the knee OA and hip OA demonstrated similar self-report outcomes (KOOS/HOOS), exhibited ranges of motion aligned with previous moderate OA groups, and met the same functional criteria, it could be postulated that the hip OA group was of a more radiographically severe disease stage, which has previously shown to influence knee joint biomechanics and neuromuscular activations.[67] Additionally, using MVICs as a method for normalization has been previously questioned regarding OA participants' ability to elicit a maximal voluntary effort due to pain and inhibition,[48,66] however studies have found that with standardized procedures and consistent feedback individuals with knee OA can recruit to similar maximum percentages as healthy controls.[222] Lastly, the treadmill speed was set to participant's self-selected walking speed as determined from the GaitRITE walkway. The assumption was made that similar gait characteristics would be adopted after a period of familiarization.[175,223] Although the GaitRITE walkway has shown excellent validity and reliability,[181] a few of the participants made comments that the treadmill initially felt faster than the speed they were walking overground despite the same velocity, although this sensation reduced after the first few minutes of walking.

5.7 Future Implications

This thesis brought a novel perspective to the study of biomechanical and neuromuscular features commonly identified in knee OA gait. To our knowledge, no other study exists comparing individuals of moderate knee OA, moderate hip OA, and

asymptomatic controls in the context of analyzing knee biomechanics and muscle activations and their uniqueness to the knee OA process. However, there are many future directions to take following this study. The findings of this thesis lay the groundwork for future investigation in the following areas:

1. This study suggests individuals with hip OA demonstrate a reduction in KAM measures in comparison to both individuals with knee OA, and asymptomatic knees. To explore the reason for this, it is important to take into consideration features such as movements that may be occurring about the hip and the trunk, static and dynamic alignment of the lower extremities, and/or measures of joint instability, and how they may be impacting joint loads at the knee.
2. As joint biomechanics are closely related to spatiotemporal measures, further investigation into how these measures differ between individuals with knee OA and a group of individuals with another lower extremity pathology, such as hip OA, may shed more light onto the uniqueness of the features of knee OA gait.
3. This study suggests differences in neuromuscular activations and frontal plane mechanics exist between groups of individuals with moderate knee OA, moderate hip OA, and age, sex, and velocity matched controls. However, whether these differences would remain, or how they change with increasing OA severity remains yet to be determined. Future studies should investigate the uniqueness of these biomechanical and neuromuscular features of knee OA gait in knee and hip OA participants of more advanced disease states.

5.8 Concluding Remarks

The main aim of this thesis was to understand whether specific biomechanical and neuromuscular gait outcomes previously linked to symptomatic medial compartment knee OA severity and progression are in fact unique to those with knee OA by concurrently investigating a group of asymptomatic individuals and those with moderate hip OA, with each comparator group having no known knee OA. It has been found that hamstring muscle activation is affected by hip OA in a direction opposite to that commonly described in knee OA, and unlike the other biomechanical and neuromuscular outcomes measured in this study, provide a gait outcome that is unique in the knee OA disease. In the other features of sagittal plane motion, moments, and KAM, similarities either exist in between hip OA and knee OA (sagittal plane moments), or asymptomatic and knee OA (KAM) or all three groups (sagittal pane motion). Identifying distinct pathomechanical alterations linked to knee OA presence and progression is crucial to continue the evolution of effective management and treatment strategies, and determining gait similarities in individuals with hip OA and knee OA may help towards developing prevention efforts for subsequent OA diagnoses.

References

1. Bombardier C (Arthritis A of C. The impact of arthritis in Canada: today and over the next 30 years. *Arthritis Alliance of Canada*. 2011;Fall:52.

2. Dillon CF, Rasch EK, Gu Q, Hirsch R. Prevalence of knee osteoarthritis in the United States: Arthritis data from the Third National Health and Nutrition Examination Survey 1991-94. *J Rheumatol*. 2006;33(11):2271-2279.

3. Egloff C, Hügle T, Valderrabano V. Biomechanics and pathomechanisms of osteoarthritis. *Swiss Med Wkly*. 2012;142(JULY):1-14. doi:10.4414/smw.2012.13583

4. Gupta KB, Duryea J, Weissman BN. Radiographic evaluation of osteoarthritis. *Radiol Clin North Am*. 2004;42(1):11-41. doi:10.1016/S0033-8389(03)00169-6

5. March LM, Bachmeier CJM. Economics of osteoarthritis: A global perspective. *Baillieres Clin Rheumatol*. 1997;11(4):817-834. doi:10.1016/S0950-3579(97)80011-8

6. Stamm TA, Pieber K, Crevenna R, Dorner TE. Impairment in the activities of daily living in older adults with and without osteoporosis, osteoarthritis and chronic back pain: A secondary analysis of population-based health survey data. *BMC Musculoskelet Disord*. 2016;17(1). doi:10.1186/s12891-016-0994-y

7. Li X, Gignac MAM, Anis AH. The indirect costs of arthritis resulting from unemployment, reduced performance, and occupational changes while at work. *Med Care*. 2006;44(4):304-310. doi:10.1097/01.mlr.0000204257.25875.04

8. Gignac MAM, Cao X, Lacaille D, Anis AH, Badley EM. Arthritis-related work transitions: A prospective analysis of reported productivity losses, work changes, and leaving the labor force. *Arthritis Care Res*. 2008;59(12):1805-1813. doi:10.1002/art.24085

9. Sharif B, Garner R, Hennessy D, Sanmartin C, Flanagan WM, Marshall DA. Productivity costs of work loss associated with osteoarthritis in Canada from 2010 to 2031. *Osteoarthr Cartil*. 2017;25(2):249-258. doi:10.1016/j.joca.2016.09.011

10. Sharif B, Kopec JA, Wong H, Anis AH. Distribution and Drivers of Average Direct Cost of Osteoarthritis in Canada From 2003 to 2010. *Arthritis Care Res*. 2017;69(2):243-251. doi:10.1002/acr.22933

11. Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthr Cartil*. 2019;27(11):1578-1589. doi:10.1016/j.joca.2019.06.011

12. Sakellariou G, Conaghan PG, Zhang W, et al. EULAR recommendations for the use of imaging in the clinical management of peripheral joint osteoarthritis. *Ann Rheum Dis*. 2017;76(9):1484-1494. doi:10.1136/annrheumdis-2016-210815

13. Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. *Arthritis Care Res*. 2020;72(2):149-162. doi:10.1002/acr.24131

14. Katz JN, Arant KR, Loeser RF. Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review. *JAMA - J Am Med Assoc*. 2021;325(6):568-578. doi:10.1001/jama.2020.22171

15. Andriacchi TP, Mündermann A. The role of ambulatory mechanics in the initiation and progression of knee osteoarthritis. *Curr Opin Rheumatol*. 2006;18(5):514-518. doi:10.1097/01.bor.0000240365.16842.4e

16. Felson DT. Osteoarthritis as a disease of mechanics. *Osteoarthr Cartil*. 2013;21(1):10-15. doi:10.1016/j.joca.2012.09.012

17. Vincent HK, Ph D. Perspective on the Knee Joint. *Pm R*. 2013;4(5 0):1-11. doi:10.1016/j.pmrj.2012.01.020.

18. Wilson DR, McWalter EJ, Johnston JD. The Measurement of Joint Mechanics and Their Role in Osteoarthritis Genesis and Progression. *Rheum Dis Clin North Am*. 2013;39(1):21-44. doi:10.1016/j.rdc.2012.11.002

19. Martel-Pelletier J. Pathophysiology of osteoarthritis. *Osteoarthr Cartil*. 2004;12(SUPLL.):31-33. doi:10.1016/j.joca.2003.10.002

20. Schofield DJ, Shrestha RN, Percival R, Passey ME, Callander EJ, Kelly SJ. The personal and national costs of lost labour force participation due to arthritis: An economic study. *BMC Public Health*. 2013;13(1):1. doi:10.1186/1471-2458-13-188

21. Tarride JE, Haq M, O'Reilly DJ, et al. The excess burden of osteoarthritis in the province of Ontario, Canada. *Arthritis Rheum*. 2012;64(4):1153-1161. doi:10.1002/art.33467

22. King LK, Kendzerska T, Waugh EJ, Hawker GA. Impact of Osteoarthritis on Difficulty Walking: A Population-Based Study. *Arthritis Care Res*. 2018;70(1):71-79. doi:10.1002/acr.23250

23. Astephen JL, Deluzio KJ, Caldwell GE, Dunbar MJ, Hubley-Kozey CL. Gait and neuromuscular pattern changes are associated with differences in knee osteoarthritis severity levels. *J Biomech*. 2008;41(4):868-876. doi:10.1016/j.jbiomech.2007.10.016

24. Childs JD, Sparto PJ, Fitzgerald GK, Bizzini M, Irrgang JJ. Alterations in lower extremity movement and muscle activation patterns in individuals with knee osteoarthritis. *Clin Biomech*. 2004;19(1):44-49. doi:10.1016/j.clinbiomech.2003.08.007

25. Heiden TL, Lloyd DG, Ackland TR. Knee joint kinematics, kinetics and muscle co-contraction in knee osteoarthritis patient gait. *Clin Biomech*. 2009;24(10):833-841. doi:10.1016/j.clinbiomech.2009.08.005

26. Mündermann A, Dyrby CO, Andriacchi TP. Secondary gait changes in patients with medial compartment knee osteoarthritis: Increased load at the ankle, knee, and hip during walking. *Arthritis Rheum*. 2005;52(9):2835-2844. doi:10.1002/art.21262

27. Nagano Y, Naito K, Saho Y, et al. Association between in vivo knee kinematics during gait and the severity of knee osteoarthritis. *Knee*. 2012;19(5):628-632. doi:10.1016/j.knee.2011.11.002

28. Rutherford D, Baker M, Wong I, Stanish W. The effect of age and knee osteoarthritis on muscle activation patterns and knee joint biomechanics during dual belt treadmill gait. *J Electromyogr Kinesiol*. 2017;34:58-64. doi:10.1016/j.jelekin.2017.04.001

29. Rudolph KS, Schmitt LC, Lewek MD. Age-related changes in strength, joint laxity, and walking patterns: Are they related to knee osteoarthritis? *Phys Ther*. 2007;87(11):1422-1432. doi:10.2522/ptj.20060137

30. Baliunas AJ, Hurwitz DE, Ryals AB, et al. Increased knee joint loads during walking are present in subjects with knee osteoarthritis. *Osteoarthr Cartil*. 2002;10(7):573-579. doi:10.1053/joca.2002.0797

31. Hatfield GL, Stanish WD, Hubley-Kozey CL. Three-dimensional biomechanical gait characteristics at baseline are associated with progression to total knee arthroplasty. *Arthritis Care Res*. 2015;67(7):1004-1014. doi:10.1002/acr.22564

32. Kaufman KR, Hughes C, Morrey BF, Morrey M, An KN. Gait characteristics of patients with knee osteoarthritis. *J Biomech*. 2001;34(7):907-915. doi:10.1016/S0021-9290(01)00036-7

33. Landry SC, McKean KA, Hubley-Kozey CL, Stanish WD, Deluzio KJ. Knee biomechanics of moderate OA patients measured during gait at a self-selected and fast walking speed. *J Biomech*. 2007;40(8):1754-1761. doi:10.1016/j.jbiomech.2006.08.010

34. Sharma L, Hurwitz DE, Thonar EJMA, et al. Knee adduction moment, serum hyaluronan level, and disease severity in medial tibiofemoral osteoarthritis. *Arthritis Rheum*. 1998;41(7):1233-1240. doi:10.1002/1529-0131(199807)41:7<1233::AID-ART14>3.0.CO;2-L

35. Constantinou M, Loureiro A, Carty C, Mills P, Barrett R. Hip joint mechanics during walking in individuals with mild-to-moderate hip osteoarthritis. *Gait Posture*. 2017;53:162-167. doi:10.1016/j.gaitpost.2017.01.017

36. Eitzen I, Fernandes L, Kalleru H, Nordsletten L, Knarr B, Risberg MA. Gait characteristics, symptoms, and function in persons with hip osteoarthritis: A longitudinal study with 6 to 7 years of follow-up. *J Orthop Sports Phys Ther*. 2015;45(7):539-549. doi:10.2519/jospt.2015.5441

37. Meyer CAG, Corten K, Fieuws S, et al. Biomechanical gait features associated with hip osteoarthritis: Towards a better definition of clinical hallmarks. *J Orthop Res*. 2015;33(10):1498-1507. doi:10.1002/jor.22924

38. Ornetti P, Laroche D, Morisset C, Beis JN, Tavernier C, Maillefert JF. Three-dimensional kinematics of the lower limbs in hip osteoarthritis during walking. *J Back Musculoskelet Rehabil*. 2011;24(4):201-208. doi:10.3233/BMR-2011-0295

39. Eitzen I, Fernandes L, Nordsletten L, Risberg MA. Sagittal plane gait characteristics in hip osteoarthritis patients with mild to moderate symptoms compared to healthy controls: A cross-sectional study. *BMC Musculoskelet Disord*. 2012;16(1):1-13. doi:10.1186/s12891-015-0483-8

40. Manal K, Gardinier E, Buchanan TS, Snyder-Mackler L. A more informed evaluation of medial compartment loading: The combined use of the knee adduction and flexor moments. *Osteoarthr Cartil*. 2015;23(7):1107-1111. doi:10.1016/j.joca.2015.02.779

41. Schipplein OD, Andriacchi TP. Interaction between active and passive knee stabilizers during level walking. *J Orthop Res*. 1991;9(1):113-119. doi:10.1002/jor.1100090114

42. Mündermann A, Dyrby CO, Hurwitz DE, Sharma L, Andriacchi TP. Potential Strategies to Reduce Medial Compartment Loading in Patients With Knee Osteoarthritis of Varying Severity: Reduced Walking Speed. *Arthritis Rheum*. 2004;50(4):1172-1178. doi:10.1002/art.20132

43. Miyazaki T, Wada M, Kawahara H, Sato M, Baba H, Shimada S. Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. *Ann Rheum Dis*. 2002;61(7):617-622. doi:10.1136/ard.61.7.617

44. Bennell KL, Bowles KA, Wang Y, Cicuttini F, Davies-Tuck M, Hinman RS. Higher dynamic medial knee load predicts greater cartilage loss over 12 months in medial knee osteoarthritis. *Ann Rheum Dis*. 2011;70(10):1770-1774. doi:10.1136/ard.2010.147082

45. Chehab EF, Favre J, Erhart-hledik JC, et al. Baseline knee adduction and flexion moments during walking are both associated with five year cartilage changes in patients with medial knee osteoarthritis. *Osteoarthr Cartil*. 2014;22(11):1833-1839. doi:10.1016/j.joca.2014.08.009.

46. Hubley-Kozey CL, Deluzio KJ, Landry SC, McNutt JS, Stanish WD. Neuromuscular alterations during walking in persons with moderate knee osteoarthritis. *J Electromyogr Kinesiol*. 2006;16(4):365-378. doi:10.1016/j.jelekin.2005.07.014

47. Hubley-Kozey CL, Hill NA, Rutherford DJ, Dunbar MJ, Stanish WD. Co-activation differences in lower limb muscles between asymptomatic controls and those with varying degrees of knee osteoarthritis during walking. *Clin Biomech*. 2009;24(5):407-414. doi:10.1016/j.clinbiomech.2009.02.005

48. Hubley-Kozey C, Deluzio K, Dunbar M. Muscle co-activation patterns during walking in those with severe knee osteoarthritis. *Clin Biomech*. 2008;23(1):71-80. doi:10.1016/j.clinbiomech.2007.08.019

49. Lynn SK, Costigan PA. Effect of foot rotation on knee kinetics and hamstring activation in older adults with and without signs of knee osteoarthritis. *Clin Biomech*. 2008;23(6):779-786. doi:10.1016/j.clinbiomech.2008.01.012

50. Schmitt LC, Rudolph KS. Influences on knee movement strategies during walking in persons with medial knee osteoarthritis. *Arthritis Care Res*. 2007;57(6):1018-1026. doi:10.1002/art.22889

51. Rutherford DJ, Hubley-Kozey CL, Stanish WD, Dunbar MJ. Neuromuscular alterations exist with knee osteoarthritis presence and severity despite walking velocity similarities. *Clin Biomech*. 2011;26(4):377-383. doi:10.1016/j.clinbiomech.2010.11.018

52. Zeni JA, Rudolph K, Higginson JS. Alterations in quadriceps and hamstrings coordination in persons with medial compartment knee osteoarthritis. *J Electromyogr Kinesiol*. 2010;20(1):148-154. doi:10.1016/j.jelekin.2008.12.003

53. Rutherford D, Baker M. Lateral to medial hamstring activation ratio: Individuals with medial compartment knee osteoarthritis compared to asymptomatic controls during gait. *Gait Posture*. 2019;70:95-97. doi:10.1016/j.gaitpost.2019.02.026

54. Van Tunen JAC, Dell'Isola A, Juhl C, et al. Association of malalignment, muscular dysfunction, proprioception, laxity and abnormal joint loading with tibiofemoral knee osteoarthritis - A systematic review and meta-analysis. *BMC Musculoskelet Disord*. 2018;19(1). doi:10.1186/s12891-018-2202-8

55. Chang A, Hayes K, Dunlop D, et al. Thrust during ambulation and the progression of knee osteoarthritis. *Arthritis Rheum*. 2004;50(12):3897-3903. doi:10.1002/art.20657

56. Chang A, Hochberg M, Song J, et al. Frequency of Varus and Valgus Thrust and Factors Associated with Thrust Presence in Persons With or at Higher Risk for Knee Osteoarthritis. *Arthritis Rheum*. 2010;62(5):1403-1411. doi:10.1002/art.27377.

57. Mahmoudian A, van Dieen JH, Bruijn SM, et al. Varus thrust in women with early medial knee osteoarthritis and its relation with the external knee adduction moment. *Clin Biomech*. 2016;39:109-114. doi:10.1016/j.clinbiomech.2016.10.006

58. Jones M, Stanish W, Rutherford D. Co-activation is not altered in the contra-lateral limb of individuals with moderate knee osteoarthritis compared to healthy controls. *Clin Biomech*. 2018;59(September):71-77. doi:10.1016/j.clinbiomech.2018.09.003

59. Rutherford DJ, Moreside J, Wong I. Differences in Hip Joint Biomechanics and Muscle Activation in Individuals With Femoroacetabular Impingement Compared With Healthy, Asymptomatic Individuals: Is Level-Ground Gait Analysis Enough? *Orthop J Sport Med*. 2018;6(5):1-10. doi:10.1177/2325967118769829

60. Allen KD, Golightly YM. Epidemiology of osteoarthritis: state of the evidence. *Curr Opin Rheumatol*. 2015;27(3):276-283. doi:10.1097/BOR.0000000000000161

61. Arden N, Nevitt MC. Osteoarthritis: Epidemiology. *Best Pract Res Clin Rheumatol*. 2006;20(1):3-25. doi:10.1016/j.berh.2005.09.007

62. Shakoor N, Block JA, Shott S, Case JP. Nonrandom evolution of end-stage osteoarthritis of the lower limbs. *Arthritis Rheum*. 2002;46(12):3185-3189. doi:10.1002/art.10649

63. Shakoor N, Hurwitz DE, Block JA, Shott S, Case JP. Asymmetric knee loading in advanced unilateral hip osteoarthritis. *Arthritis Rheum*. 2003;48(6):1556-1561. doi:10.1002/art.11034

64. Gillam MH, Lie SA, Salter A, et al. The progression of end-stage osteoarthritis: Analysis of data from the Australian and Norwegian joint replacement registries using a multi-state model. *Osteoarthr Cartil*. 2013;21(3):405-412. doi:10.1016/j.joca.2012.12.008

65. Jungmann PM, Nevitt MC, Baum T, et al. Relationship of Unilateral Total Hip Arthroplasty (THA) to Contralateral and Ipsilateral Knee Joint Degeneration: A Longitudinal 3T MRI Study from the Osteoarthritis Initiative (OAI). *Osteoarthr Cartil*. 2015;23(7):1144-1153. doi:10.1016/j.joca.2015.03.022.

66. Rutherford D, Moreside J, Wong I. Knee joint motion and muscle activation patterns are altered during gait in individuals with moderate hip osteoarthritis compared to asymptomatic cohort. *Clin Biomech*. 2015;30(6):578-584. doi:10.1016/j.clinbiomech.2015.04.002

67. Rutherford D, Buckingham L, Moreside J, Wong I, Richardson G. Knee motion and muscle activation patterns are altered in hip osteoarthritis: The effect of severity on walking mechanics. *Clin Biomech*. 2018;59(August):1-7. doi:10.1016/j.clinbiomech.2018.08.001

68. Wittenauer R, Smith L, Aden K. *Update on 2004 Background Paper Background Paper 6 . 12 Osteoarthritis*.; 2013.

69. Kraus VB, Blanco FJ, Englund M, Karsdal MA, Lohmander LS. Call for Standardized Definitions of Osteoarthritis and Risk Stratification for Clinical Trials and Clinical Use. *Osteoarthr Cartil*. 2015;23(8):1233-1241. doi:10.1016/j.joca.2015.03.036.

70. Altman R, Asch E, Bloch D, et al. Development of criteria for the classification and reporting of osteoarthritis: Classification of osteoarthritis of the knee. *Arthritis Rheum*. 1986;29(8):1039-1049. doi:10.1002/art.1780290816

71. Zhang W, Doherty M, Peat G, et al. EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. *Ann Rheum Dis*. 2010;69(3):483-489. doi:10.1136/ard.2009.113100

72. Anandacoomarasamy A, March L. Current evidence for osteoarthritis treatments. *Ther Adv Musculoskelet Dis*. 2010;2(1):17-28. doi:10.1177/1759720X09359889

73. Farr JN, Going SB, Lohman TG, et al. Physical activity levels in patients with early knee osteoarthritis measured by accelerometry. *Arthritis Care Res*. 2008;59(9):1229-1236. doi:10.1002/art.24007

74. Cassell EJ. *The Healer's Art: A New Approach to the Doctor-Patient Relationship*. Harmondsworth, Eng.: Penguin Books; 1976.

75. Eisenberg L. Disease and illness Distinctions between professional and popular ideas of sickness. *Cult Med Psychiatry*. 1977;1(1):9-23. doi:10.1007/BF00114808

76. Schmitt D, Vap A, Queen RM. Effect of end-stage hip, knee, and ankle osteoarthritis on walking mechanics. *Gait Posture*. 2015;42(3):373-379. doi:10.1016/j.gaitpost.2015.07.005

77. Metcalfe AJ, Andersson M Le, Goodfellow R, Thorstensson CA. Is knee osteoarthritis a symmetrical disease? Analysis of a 12year prospective cohort study. *BMC Musculoskelet Disord*. 2012;13. doi:10.1186/1471-2474-13-153

78. Spector TD, Hart DJ, Doyle D V. Incidence and progression of osteoarthritis in women with unilateral knee disease in the general population: The effect of obesity. *Ann Rheum Dis*. 1994;53(9):565-568. doi:10.1136/ard.53.9.565

79. Chitnavis J, Sinsheimer JS, Suchard MA, Clipsham K, Carr AJ. End-stage coxarthrosis and gonarthrosis. Aetiology, clinical patterns and radiological features of idiopathic osteoarthritis. *Rheumatology*. 2000;39(6):612-619. doi:10.1093/rheumatology/39.6.612

80. Schmidt A, Meurer A, Lenarz K, et al. Unilateral hip osteoarthritis: The effect of compensation strategies and anatomic measurements on frontal plane joint loading. *J Orthop Res*. 2017;35(8):1764-1773. doi:10.1002/jor.23444

81. Hawker GA, Badley EM, Croxford R, et al. A population-based nested case-control study of the costs of hip and knee replacement surgery. *Med Care*. 2009;47(7):732-741. doi:10.1097/MLR.0b013e3181934553

82. CJRR annual report: Hip and knee replacements in Canada. CIHI.

83. Inacio MCS, Paxton EW, Graves SE, Namba RS, Nemes S. Projected increase in total knee arthroplasty in the United States – an alternative projection model. *Osteoarthr Cartil*. 2017;25(11):1797-1803. doi:10.1016/j.joca.2017.07.022

84. Sharif B, Kopec J, Bansback N, et al. Projecting the direct cost burden of osteoarthritis in Canada using a microsimulation model. *Osteoarthr Cartil*. 2015;23(10):1654-1663. doi:10.1016/j.joca.2015.05.029

85. Calders P, Van Ginckel A. Presence of comorbidities and prognosis of clinical symptoms in knee and/or hip osteoarthritis: A systematic review and meta-analysis. *Semin Arthritis Rheum*. 2018;47(6):805-813. doi:10.1016/j.semarthrit.2017.10.016

86. Wise BL, Niu J, Yang M, et al. Patterns of Compartment Involvement in Tibiofemoral Osteoarthritis in Men and Women and in Caucasians and African Americans: the Multicenter Osteoarthritis Study. *Arthritis Care Res*. 2012;64(6):847-852. doi:10.1002/acr.21606.

87. Mesci E. Relation of physical activity level with quality of life, sleep and depression in patients with knee osteoarthritis. *North Clin Istanbul*. 2015;2(3):215-221. doi:10.14744/nci.2015.95867

88. Ross R, Chaput JP, Giangregorio LM, et al. Canadian 24-Hour Movement Guidelines for Adults aged 18-64 years and Adults aged 65 years or older: an integration of physical activity, sedentary behaviour, and sleep. *Appl Physiol Nutr Metab*. 2020;45(10):S57-S102. doi:10.1139/apnm-2020-0467

89. Lee J, Song J, Hootman JM, et al. Obesity and other modifiable factors for physical inactivity measured by accelerometer in adults with knee osteoarthritis. *Arthritis Care Res*. 2013;65(1):53-61. doi:10.1002/acr.21754

90. Herbolsheimer F, Schaap LA, Edwards MH, et al. Physical Activity Patterns among Older Adults with and Without Knee Osteoarthritis in Six European Countries. *Arthritis Care Res*. 2016;68(2):228-236. doi:10.1002/acr.22669

91. Stubbs B, Hurley M, Smith T. What are the factors that influence physical activity participation in adults with knee and hip osteoarthritis? A systematic review of physical activity correlates. *Clin Rehabil*. 2015;29(1):80-94. doi:10.1177/0269215514538069

92. *Life with Arthritis in Canada: A Personal and Public Health Challenge*.; 2010.

93. Branche PMOKO-SJHAA. *International Classififcation of Functioning, Disability and Health*.; 2001.

94. Jette AM. Toward a common language for function, disability, and health. *Phys Ther*. 2006;86(5):726-734. doi:10.1093/ptj/86.5.726

95. Dreinhöfer K, Stucki G, Ewert T, et al. ICF Core Sets for osteoarthritis. *J Rehabil Med Suppl*. 2004;(44):75-80. doi:10.1080/16501960410015498

96. Neufeld S, Machacova K, Mossey J, Luborsky M. Walking Ability and Its Relationship to Self-Rated Health in Later Life. *Clin Gerontol*. 2013;36(1):17-32. doi:10.1080/07317115.2012.731477

97. 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(1):233. doi:10.1186/1471-2474-11-233

98. Sliepen M, Mauricio E, Lipperts M, Grimm B, Rosenbaum D. Objective assessment of physical activity and sedentary behaviour in knee osteoarthritis patients - Beyond daily steps and total sedentary time. *BMC Musculoskelet Disord*. 2018;19(1):1-10. doi:10.1186/s12891-018-1980-3

99. Minor MA. Exercise in the treatment of osteoarthritis. *Rheum Dis Clin North Am*. 1999;25(2):520-523. doi:10.1007/s11926-001-0067-5

100. Lee O, Lee DC, Lee S, Kim YS. Associations between physical activity and obesity defined by Waist-To-Height ratio and body mass index in the Korean population. *PLoS One*. 2016;11(7):1-12. doi:10.1371/journal.pone.0158245

101. Brandt KD, Dieppe P, Radin EL. Etiopathogenesis of Osteoarthritis. *Rheum Dis Clin North Am*. 2008;34(3):531-559. doi:10.1016/j.rdc.2008.05.011

102. Favre J, Jolles BM. Gait analysis of patients with knee osteoarthritis highlights a pathological mechanical pathway and provides a basis for therapeutic interventions. *EFORT Open Rev*. 2016;1(10):368-374. doi:10.1302/2058-5241.1.000051

103. Andriacchi TP, Mündermann A, Smith RL, Alexander EJ, Dyrby CO, Koo S. A framework for the in vivo pathomechanics of osteoarthritis at the knee. *Ann Biomed Eng*. 2004;32(3):447-457. doi:10.1023/B:ABME.0000017541.82498.37

104. Baker R. Gait analysis methods in rehabilitation. *J Neuroeng Rehabil*. 2006;3:1-10. doi:10.1186/1743-0003-3-4

105. Muro-de-la-Herran A, García-Zapirain B, Méndez-Zorrilla A. Gait analysis methods: An overview of wearable and non-wearable systems, highlighting clinical applications. *Sensors (Switzerland)*. 2014;14(2):3362-3394. doi:10.3390/s140203362

106. Murphy MA, Sunnerhagen KS, Johnels B, Willén C. Three-dimensional kinematic motion analysis of a daily activity drinking from a glass: A pilot study. *J Neuroeng Rehabil*. 2006;3:1-11. doi:10.1186/1743-0003-3-18

107. Dixon SJ, Hinman RS, Creaby MW, Kemp G, Crossley KM. Knee joint stiffness during walking in knee osteoarthritis. *Arthritis Care Res*. 2010;62(1):38-44. doi:10.1002/acr.20012

108. Lewek MD, Scholz J, Rudolph KS, Snyder-Mackler L. Stride-to-stride variability of knee motion in patients with knee osteoarthritis. *Gait Posture*. 2006;23(4):505-511. doi:10.1016/j.gaitpost.2005.06.003

109. Abid M, Mezghani N, Mitiche A. Knee joint biomechanical gait data classification for knee pathology assessment: A literature review. *Appl Bionics Biomech*. 2019;2019. doi:10.1155/2019/7472039

110. Farrokhi S, O'Connell M, Gil AB, Sparto PJ, Fitzgerald GK. Altered gait characteristics in individuals with knee osteoarthritis and self-reported knee instability. *J Orthop Sports Phys Ther*. 2015;45(5):351-359. doi:10.2519/jospt.2015.5540

111. Butler RJ, Barrios JA, Royer T, Davis IS. Frontal-plane gait mechanics in people with medial knee osteoarthritis are different from those in people with lateral knee osteoarthritis. *Phys Ther*. 2011;91(8):1235-1243. doi:10.2522/ptj.20100324

112. Komnik I, David S, Funken J, Haberer C, Potthast W, Weiss S. Compromised knee internal rotation in total knee arthroplasty patients during stair climbing. *PLoS One*. 2018;13(10):e0205492. doi:10.1371/journal.pone.0205492

113. Hunt MA, Charlton JM, Felson DT, et al. Frontal plane knee alignment mediates the effect of frontal plane rearfoot motion on knee joint load distribution during walking in people with medial knee osteoarthritis. *Osteoarthr Cartil*. 2021;29(5):678-686. doi:10.1016/j.joca.2021.02.003

114. Weidow J, Tranberg R, Saari T, Ka¨rrholm J. Hip and Knee Joint Rotations Differ between Patients with Medial and Lateral Knee Osteoarthritis: Gait Analysis of 30 Patients and 15 Controls. *J Orthop Res Sept 2006*. 2006.

115. Ramsey DK, Wretenberg PF. Biomechanics of the knee: Methodological considerations in the in vivo kinematic analysis of the tibiofemoral and patellofemoral joint. *Clin Biomech*. 1999;14(9):595-611. doi:10.1016/S0268-0033(99)00015-7

116. Della Croce U, Leardini A, Chiari L, Cappozzo A. Human movement analysis using stereophotogrammetry Part 4: Assessment of anatomical landmark misplacement and its effects on joint kinematics. *Gait Posture*. 2005;21(2):226-237. doi:10.1016/j.gaitpost.2004.05.003

117. Leardini A, Chiari A, Della Croce U, Cappozzo A. Human movement analysis using stereophotogrammetry Part 3. Soft tissue artifact assessment and compensation. *Gait Posture*. 2005;21(2):212-225. doi:10.1016/j.gaitpost.2004.05.002

118. Chiari L, Della Croce U, Leardini A, Cappozzo A. Human movement analysis using stereophotogrammetry. Part 2: Instrumental errors. *Gait Posture*. 2005;21(2):197-211. doi:10.1016/j.gaitpost.2004.04.004

119. Rutherford DJ, Moyer R, Baker M, Saleh S. High day-to-day repeatability of lower extremity muscle activation patterns and joint biomechanics of dual-belt treadmill gait: A reliability study in healthy young adults. *J Electromyogr Kinesiol*. 2020;51(February):102401. doi:10.1016/j.jelekin.2020.102401

120. Sun HB. Mechanical loading, cartilage degradation, and arthritis. *Ann N Y Acad Sci*. 2010;1211:37-50. doi:10.1111/j.1749-6632.2010.05808.x

121. D'Lima DD, Fregly BJ, Patil S, Steklov N, Colwell CW. Knee joint forces: Prediction, measurement, and significance. *Proc Inst Mech Eng Part H J Eng Med*. 2012;226(2):95-102. doi:10.1177/0954411911433372

122. Zheng H, Chen C. Body mass index and risk of knee osteoarthritis: Systematic review and meta-analysis of prospective studies. *BMJ Open*. 2015;5(12). doi:10.1136/bmjopen-2014-007568

123. McGinnis PM. *Biomechanics of Sport and Exercise*. 3rd ed. Champaign, IL: Human Kinetics; 2013.

124. Rutherford DJ, Baker M. Knee moment outcomes using inverse dynamics and the cross product function in moderate knee osteoarthritis gait: A comparison study. *J Biomech*. 2018;78:150-154. doi:10.1016/j.jbiomech.2018.07.021

125. Henriksen M, Creaby MW, Lund H, Juhl C, Christensen R. Is there a causal link between knee loading and knee osteoarthritis progression? A systematic review and meta-analysis of cohort studies and randomised trials. *BMJ Open*. 2014;4(7):1-9. doi:10.1136/bmjopen-2014-005368

126. Walter JP, D'Lima DD, Colwell CW, Fregly BJ. Decreased knee adduction moment does not guarantee decreased medial contact force during gait. *J Orthop Res*. 2010;28(10):1348-1354. doi:10.1002/jor.21142

127. Eng JJ, Winter DA. Kinetic analysis of the lower limbs during walking: What information can be gained from a three-dimensional model? *J Biomech*. 1995;28(6):753-758. doi:10.1016/0021-9290(94)00124-M

128. Huang SC, Wei IP, Chien HL, et al. Effects of severity of degeneration on gait patterns in patients with medial knee osteoarthritis. *Med Eng Phys*. 2008;30(8):997-1003. doi:10.1016/j.medengphy.2008.02.006

129. Al-Zahrani KS, Bakheit AMO. A study of the gait characteristics of patients with chronic osteoarthritis of the knee. *Disabil Rehabil*. 2002;24(5):275-280. doi:10.1080/09638280110087098

130. Asay JL, Erhart-Hledik JC, Andriacchi TP. Changes in the total knee joint moment in patients with medial compartment knee osteoarthritis over 5 years. *J Orthop Res*. 2018;36(9):2373-2379. doi:10.1002/jor.23908

131. Brisson NM, Stratford PW, Maly MR. Relative and absolute test–retest reliabilities of biomechanical risk factors for knee osteoarthritis progression: benchmarks for meaningful change. *Osteoarthr Cartil*. 2018;26(2):220-226. doi:10.1016/j.joca.2017.11.003

132. Gustafson JA, Robinson ME, Fitzgerald GK, Tashman S, Farrokhi S. Knee motion variability in patients with knee osteoarthritis: The effect of self-reported instability. *Clin Biomech*. 2015;30(5):475-480. doi:10.1016/j.clinbiomech.2015.03.007

133. Lewek MD, Rudolph KS, Snyder-Mackler L. Control of frontal plane knee laxity during gait in patients with medial compartment knee osteoarthritis. *Osteoarthr Cartil*. 2004;12(9):745-751. doi:10.1016/j.joca.2004.05.005

134. Zeni JA, Higginson JS. Differences in gait parameters between healthy subjects and persons with moderate and severe knee osteoarthritis: A result of altered walking speed? *Clin Biomech*. 2009;24(4):372-378. doi:10.1016/j.clinbiomech.2009.02.001

135. Kutzner I, Trepczynski A, Heller MO, Bergmann G. Knee adduction moment and medial contact force-facts about their correlation during gait. *PLoS One*. 2013;8(12):8-15. doi:10.1371/journal.pone.0081036

136. Maly MR. Linking biomechanics to mobility and disability in people with knee osteoarthritis. *Exerc Sport Sci Rev*. 2008;37(1):36-42. doi:10.1097/JES.0b013e3181912071

137. Andriacchi TP. Dynamics of knee malalignment. *Orthop Clin North Am*. 1994;25(3):395-403.

138. Kean CO, Hinman RS, Bowles KA, Cicuttini F, Davies-Tuck M, Bennell KL. Comparison of peak knee adduction moment and knee adduction moment impulse in distinguishing between severities of knee osteoarthritis. *Clin Biomech*. 2012;27(5):520-523. doi:10.1016/j.clinbiomech.2011.12.007

139. Robbins SMK, Maly MR. The effect of gait speed on the knee adduction moment depends on waveform summary measures. *Gait Posture*. 2009;30(4):543-546. doi:10.1016/j.gaitpost.2009.08.236

140. Thorp LE, Sumner DR, Block JA, Moisio KC, Shott S, Wimmer MA. Knee joint loading differs in individuals with mild compared with moderate medial knee osteoarthritis. *Arthritis Rheum*. 2006;54(12):3842-3849. doi:10.1002/art.22247

141. Creaby MW, Wang Y, Bennell KL, et al. Dynamic knee loading is related to cartilage defects and tibial plateau bone area in medial knee osteoarthritis. *Osteoarthr Cartil*. 2010;18(11):1380-1385. doi:10.1016/j.joca.2010.08.013

142. Hall M, Bennell KL, Wrigley T V., et al. The knee adduction moment and knee osteoarthritis symptoms: relationships according to radiographic disease severity. *Osteoarthr Cartil*. 2017;25(1):34-41. doi:10.1016/j.joca.2016.08.014

143. Meldrum D, Shouldice C, Conroy R, Jones K, Forward M. Test-retest reliability of three dimensional gait analysis: Including a novel approach to visualising agreement of gait cycle waveforms with Bland and Altman plots. *Gait Posture*. 2014;39(1):265-271. doi:10.1016/j.gaitpost.2013.07.130

144. Robbins SM, Astephen Wilson JL, Rutherford DJ, Hubley-Kozey CL. Reliability of principal components and discrete parameters of knee angle and moment gait waveforms in individuals with moderate knee osteoarthritis. *Gait Posture*. 2013;38(3):421-427. doi:10.1016/j.gaitpost.2013.01.001

145. Panjabi MM. Panjabi 1992.pdf. *J Spinal Disord*. 1992;5:383-389.

146. Schache AG, Dorn TW, Blanch PD, Brown NAT, Pandy MG. Mechanics of the human hamstring muscles during sprinting. *Med Sci Sports Exerc*. 2012;44(4):647-658. doi:10.1249/MSS.0b013e318236a3d2

147. Zhang LQ, Xu D, Wang G, Hendrix RW. Muscle strength in knee varus and valgus. *Med Sci Sports Exerc*. 2001;33(7):1194-1199. doi:10.1097/00005768-200107000-00018

148. Lloyd DG, Buchanan TS. Strategies of muscular support of varus and valgus isometric loads at the human knee. *J Biomech*. 2001;34(10):1257-1267. doi:10.1016/S0021-9290(01)00095-1

149. Sharma SK, Yadav SL, Singh U, Wadhwa S. Muscle activation profiles and coactivation of quadriceps and hamstring muscles around knee joint in Indian primary osteoarthritis knee patients. *J Clin Diagnostic Res*. 2017;11(5):RC09-RC14. doi:10.7860/JCDR/2017/26975.9870

150. Rutherford DJ, Hubley-Kozey CL, Stanish WD. Changes in knee joint muscle activation patterns during walking associated with increased structural severity in knee osteoarthritis. *J Electromyogr Kinesiol*. 2013;23(3):704-711. doi:10.1016/j.jelekin.2013.01.003

151. Rutherford DJ, Hubley-Kozey CL, Stanish WD. The neuromuscular demands of altering foot progression angle during gait in asymptomatic individuals and those with knee osteoarthritis. *Osteoarthr Cartil*. 2010;18(5):654-661. doi:10.1016/j.joca.2010.01.005

152. Astephen Wilson JL, Deluzio KJ, Dunbar MJ, Caldwell GE, Hubley-Kozey CL. The association between knee joint biomechanics and neuromuscular control and moderate knee osteoarthritis radiographic and pain severity. *Osteoarthr Cartil*. 2011;19(2):186-193. doi:10.1016/j.joca.2010.10.020

153. Ward SR, Eng CM, Smallwood LH, Lieber RL. Are current measurements of lower extremity muscle architecture accurate? *Clin Orthop Relat Res*. 2009;467(4):1074-1082. doi:10.1007/s11999-008-0594-8

154. Kary JM. Diagnosis and management of quadriceps strains and contusions. *Curr Rev Musculoskelet Med*. 2010;3(1-4):26-31. doi:10.1007/s12178-010-9064-5

155. Perry J, Burnfield J. *Gait Analysis Normal & Pathological Function*. Thorofare, NJ.: SLACK Incorporated; 1992.

156. Stief F, Schmidt A, van Drongelen S, et al. Abnormal loading of the hip and knee joints in unilateral hip osteoarthritis persists two years after total hip replacement. *J Orthop Res*. 2018;36(8):2167-2177. doi:10.1002/jor.23886

157. Ro DH, Lee J, Lee J, Park JY, Han HS, Lee MC. Effects of Knee Osteoarthritis on Hip and Ankle Gait Mechanics. *Adv Orthop*. 2019;2019(1). doi:10.1155/2019/9757369

158. Joseph GB, Hilton JF, Jungmann PM, et al. Do persons with asymmetric hip pain or radiographic hip OA have worse pain and structure outcomes in the knee opposite the more affected hip? Data from the Osteoarthritis Initiative. *Osteoarthr Cartil*. 2016;24(3):427-435. doi:10.1016/j.joca.2015.10.001

159. Baker M, Moreside J, Wong I, Rutherford DJ. Passive hip movement measurements related to dynamic motion during gait in hip osteoarthritis. *J Orthop Res*. 2016;34(10):1790-1797. doi:10.1002/jor.23198

160. Rutherford DJ, Moreside J, Wong I. Hip joint motion and gluteal muscle activation differences between healthy controls and those with varying degrees of hip osteoarthritis during walking. *J Electromyogr Kinesiol*. 2015;25(6):944-950. doi:10.1016/j.jelekin.2015.10.010

161. Foucher KC, Wimmer MA. Contralateral hip and knee gait biomechanics are unchanged by total hip replacement for unilateral hip osteoarthritis. *Gait Posture*. 2012;35(1):61-65. doi:10.1016/j.gaitpost.2011.08.006

162. Foucher KC, Schlink BR, Shakoor N, Wimmer MA. Sagittal plane hip motion reversals during walking are associated with disease severity and poorer function in subjects with hip osteoarthritis. *J Biomech*. 2012;45(8):1360-1365. doi:10.1016/j.jbiomech.2012.03.008

163. Dicharry J. Kinematics and kinetics of gait: From lab to clinic. *Clin Sports Med*. 2010;29(3):347-364. doi:10.1016/j.csm.2010.03.013

164. Astephen JL, Deluzio KJ, Caldwell GE, Dunbar MJ. Biomechanical changes at the hip, knee, and ankle joints during gait are associated with knee osteoarthritis severity. *J Orthop Res*. 2008;26(3):332-341. doi:10.1002/jor.20496

165. Shakoor N, Dua A, Thorp LE, et al. Asymmetric loading and bone mineral density at the asymptomatic knees of patients with unilateral hip osteoarthritis. *Arthritis Rheum*. 2011;63(12):3853-3858. doi:10.1002/art.30626

166. Shakoor N, Foucher KC, Wimmer MA, Mikolaitis-Preuss RA, Fogg LF, Block JA. Asymmetries and relationships between dynamic loading, muscle strength, and proprioceptive acuity at the knees in symptomatic unilateral hip osteoarthritis. *Arthritis Res Ther*. 2014;16(1):1-8. doi:10.1186/s13075-014-0455-7

167. Schmidt A, Stief F, Lenarz K, et al. Unilateral hip osteoarthritis: Its effects on preoperative lower limb muscle activation and intramuscular coordination patterns. *Gait Posture*. 2016;45:187-192. doi:10.1016/j.gaitpost.2016.01.028

168. Perron M, Malouin F, Moffet H, McFadyen BJ. Three-dimensional gait analysis in women with a total hip arthroplasty. *Clin Biomech*. 2000;15(7):504-515. doi:10.1016/S0268-0033(00)00002-4

169. McGinley JL, Baker R, Wolfe R, Morris ME. The reliability of three-dimensional kinematic gait measurements: A systematic review. *Gait Posture*. 2009;29(3):360-369. doi:10.1016/j.gaitpost.2008.09.003

170. Schwartz MH, Trost JP, Wervey RA. Measurement and management of errors in quantitative gait data. *Gait Posture*. 2004;20(2):196-203. doi:10.1016/j.gaitpost.2003.09.011

171. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J Chiropr Med*. 2016;15(2):155-163. doi:10.1016/j.jcm.2016.02.012

172. Birmingham TB, Hunt MA, Jones IC, Jenkyn TR, Giffin JR. Test-retest reliability of the peak knee adduction moment during walking in patients with medial compartment knee osteoarthritis. *Arthritis Care Res*. 2007;57(6):1012-1017. doi:10.1002/art.22899

173. Hubley-Kozey CL, Robbins SM, Rutherford DJ, Stanish WD. Reliability of surface electromyographic recordings during walking in individuals with knee osteoarthritis. *J Electromyogr Kinesiol*. 2013;23(2):334-341. doi:10.1016/j.jelekin.2012.12.002

174. Altman R, Alarcon G, Appelrouth D, et al. The American College of Rheumatology Criteria for the classification and reporting of osteoarthritis of the hip. *Arthritis Rheum*. 1991;34(5):505-514.

175. Rutherford D, Baker M, Wong I, Stanish W. Dual-belt treadmill familiarization: Implications for knee function in moderate knee osteoarthritis compared to asymptomatic controls. *Clin Biomech*. 2017;45(July 2016):25-31. doi:10.1016/j.clinbiomech.2017.04.006

176. Arbab D, van Ochten JHM, Schnurr C, Bouillon B, König D. Assessment of reliability, validity, responsiveness and minimally important change of the German Hip dysfunction and osteoarthritis outcome score (HOOS) in patients with osteoarthritis of the hip. *Rheumatol Int*. 2017;37(12):2005-2011. doi:10.1007/s00296-017-3834-y

177. Nilsdotter AK, Stefan Lohmander L, Klässbo M, Roos EM, Stefan Lohmander - Stefan L. BMC Musculoskeletal Disorders Hip disability and osteoarthritis outcome score (HOOS) – validity and responsiveness in total hip replacement. *BMC Musculoskelet Disord*. 2003;8:1-8.

178. Collins NJ, Prinsen CAC, Christensen R, Bartels EM, Terwee CB, Roos EM. Knee Injury and Osteoarthritis Outcome Score (KOOS): systematic review and meta-analysis of measurement properties. *Osteoarthr Cartil*. 2016;24(8):1317-1329. doi:10.1016/j.joca.2016.03.010

179. Gandbhir VN, Cunha B. Goniometer. StatPearls Publishing.

180. Hermens HJ, Freriks B, Merletti R, et al. European Recommendations for Surface ElectroMyoGraphy. *Roessingh Res Dev*. 1999:8-11.

181. Menz HB, Latt MD, Tiedemann A, Kwan MMS, Lord SR. Reliability of the GAITRite® walkway system for the quantification of temporo-spatial parameters of gait in young and older people. *Gait Posture*. 2004;20(1):20-25. doi:10.1016/S0966-6362(03)00068-7

182. Dunphy C, Casey S, Lomond A, Rutherford D. Contralateral pelvic drop during gait increases knee adduction moments of asymptomatic individuals. *Hum Mov Sci*. 2016;49:27-35. doi:10.1016/j.humov.2016.05.008

183. Rutherford DJ, Hubley-Kozey CL, Stanish WD. Maximal voluntary isometric contraction exercises: A methodological investigation in moderate knee osteoarthritis. *J Electromyogr Kinesiol*. 2011;21(1):154-160. doi:10.1016/j.jelekin.2010.09.004

184. Grood ES, Suntay WJ. A joint coordinate system for the clinical description of three-dimensional motions: Application to the knee. *J Biomech Eng*. 1983;105(2):136-144. doi:10.1115/1.3138397

185. Wu G, Seigler S, Allard P, et al. ISB recommendation on definitions of joint coordinate system of various joints for the reporting of human joint motion—part I: ankle, hip, and spine. *J Biomech*. 2002;35(4):543-548.

186. Mawase F, Haizler T, Bar-Haim S, Karniel A. Kinetic adaptation during locomotion on a split-belt treadmill. *J Neurophysiol*. 2013;109(8):2216-2227. doi:10.1152/jn.00938.2012

187. Vaughan CL, Davis BL, O'Connor JC. *Dynamics of Human Gait*. 2nd ed. Cape Town, ZA: Kiboho Publishers; 1999.

188. Rutherford D, Moreside J, Wong I. Knee joint motion and muscle activation patterns are altered during gait in individuals with moderate hip osteoarthritis compared to asymptomatic cohort. *Clin Biomech*. 2015;30(6):578-584. doi:10.1016/j.clinbiomech.2015.04.002

189. Sullivan GM, Feinn R. Using Effect Size—or Why the P Value Is Not Enough . *J Grad Med Educ*. 2012;4(3):279-282. doi:10.4300/jgme-d-12-00156.1

190. Anderson AS, Loeser RF. Why is OA an age-related disease. *Best Pr Res Clin Rheumatol*. 2010;24(1):1-18. doi:10.1016/j.berh.2009.08.006.

191. Boyer KA, Andriacchi TP. The nature of age-related differences in knee function during walking: Implication for the development of knee osteoarthritis. *PLoS One*. 2016;11(12):1-12. doi:10.1371/journal.pone.0167352

192. Losina E, Weinstein AM, Reichmann WM, et al. Lifetime risk and age of diagnosis of symptomatic knee osteoarthritis in the US. *Arthritis Care Res*. 2013;65(5):1-16. doi:10.1002/acr.21898.Lifetime

193. Schimpl M, Moore C, Lederer C, et al. Association between walking speed and age in healthy, free-living individuals using mobile accelerometry-a cross-sectional study. *PLoS One*. 2011;6(8). doi:10.1371/journal.pone.0023299

194. Astephen Wilson JL. Challenges in dealing with walking speed in knee osteoarthritis gait analyses. *Clin Biomech*. 2012;27(3):210-212. doi:10.1016/j.clinbiomech.2011.09.009

195. 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):291-303. doi:10.2519/jospt.2014.4634

196. Bejek Z, Paróczai R, Illyés Á, Kiss RM. The influence of walking speed on gait parameters in healthy people and in patients with osteoarthritis. *Knee Surgery, Sport Traumatol Arthrosc*. 2006;14(7):612-622. doi:10.1007/s00167-005-0005-6

197. Hortobágyi T, Westerkamp L, Beam S, et al. Altered hamstring-quadriceps muscle balance in patients with knee osteoarthritis. *Clin Biomech*. 2005;20(1):97-104. doi:10.1016/j.clinbiomech.2004.08.004

198. Graham JE, Fisher SR, Bergés IM, Kuo YF, Ostir G V. Walking speed threshold for classifying walking independence in hospitalized older adults. *Phys Ther*. 2010;90(11):1591-1597. doi:10.2522/ptj.20100018

199. McKean KA, Landry SC, Hubley-Kozey CL, Dunbar MJ, Stanish WD, Deluzio KJ. Gender differences exist in osteoarthritic gait. *Clin Biomech*. 2007;22(4):400-409. doi:10.1016/j.clinbiomech.2006.11.006

200. Astephen Wilson JL, Dunbar MJ, Hubley-Kozey CL. Knee joint biomechanics and neuromuscular control during gait before and after total knee arthroplasty are sex-specific. *J Arthroplasty*. 2015;30(1):118-125. doi:10.1016/j.arth.2014.07.028

201. Ro DH, Lee DY, Moon G, et al. Sex differences in knee joint loading: Cross-sectional study in geriatric population. *J Orthop Res*. 2017;35(6):1283-1289. doi:10.1002/jor.23374

202. Allison K, Hall M, Wrigley T V., Pua YH, Metcalf B, Bennell KL. Sex-specific walking kinematics and kinetics in individuals with unilateral, symptomatic hip osteoarthritis: A cross sectional study. *Gait Posture*. 2018;65(April):234-239. doi:10.1016/j.gaitpost.2018.07.179

203. Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. *EClinicalMedicine*. 2020;29-30:100587. doi:10.1016/j.eclinm.2020.100587

204. Cubukcu D, Sarsan A, Alkan H. Relationships between Pain, Function and Radiographic Findings in Osteoarthritis of the Knee: A Cross-Sectional Study. *Arthritis*. 2012;2012(April 2007):1-5. doi:10.1155/2012/984060

205. Lee LS, Chan PK, Fung WC, Chan VWK, Yan CH, Chiu KY. Imaging of knee osteoarthritis: A review of current evidence and clinical guidelines. *Musculoskeletal Care*. 2021;19(3):363-374. doi:10.1002/msc.1536

206. Bedson J, Croft PR. The discordance between clinical and radiographic knee osteoarthritis: A systematic search and summary of the literature. *BMC Musculoskelet Disord*. 2008;9:1-11. doi:10.1186/1471-2474-9-116

207. Kim C, Nevitt MC, Niu J, et al. Association of hip pain with radiographic evidence of hip osteoarthritis: Diagnostic test study. *BMJ*. 2015;351. doi:10.1136/bmj.h5983

208. Soucie JM, Wang C, Forsyth A, et al. Range of motion measurements: Reference values and a database for comparison studies. *Haemophilia*. 2011;17(3):500-507. doi:10.1111/j.1365-2516.2010.02399.x

209. Hilfiker R, Jüni P, Nüesch E, Dieppe PA, Reichenbach S. Association of radiographic osteoarthritis, pain on passive movement and knee range of motion: A cross-sectional study. *Man Ther*. 2015;20(2):361-365. doi:10.1016/j.math.2014.11.014

210. van Doormaal MCM, Meerhoff GA, Vliet Vlieland TPM, Peter WF. A clinical practice guideline for physical therapy in patients with hip or knee osteoarthritis. *Musculoskeletal Care*. 2020;18(4):575-595. doi:10.1002/msc.1492

211. Fernandes L, Hagen KB, Bijlsma JWJ, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. *Ann Rheum Dis*. 2013;72(7):1125-1135. doi:10.1136/annrheumdis-2012-202745

212. Smith TO, Purdy R, Lister S, Salter C, Fleetcroft R, Conaghan PG. Attitudes of people with osteoarthritis towards their conservative management: A systematic review and meta-ethnography. *Rheumatol Int*. 2014;34(3):299-313. doi:10.1007/s00296-013-2905-y

213. Favre J, Erhart-Hledik JC, Chehab EF, Andriacchi TP. Baseline ambulatory knee kinematics are associated with changes in cartilage thickness in osteoarthritic patients over 5 years. *J Biomech*. 2016;49(9):1859-1864. doi:10.1016/j.jbiomech.2016.04.029

214. Favre J, Erhart-Hledik JC, Chehab EF, Andriacchi TP. General scheme to reduce the knee adduction moment by modifying a combination of gait variables. *J Orthop Res*. 2016;34(9):1547-1556. doi:10.1002/jor.23151

215. Harkey MS, Price LL, McAlindon TE, et al. Declining Walking Speed Associates with Increasing Bone Marrow Lesion Volume and Effusion Volume in Individuals with Accelerated Knee Osteoarthritis. *Arthritis Care Res*. 2019;71(2):259-270.

216. Astephen Wilson JL, Stanish WD, Hubley-Kozey CL. Asymptomatic and symptomatic individuals with the same radiographic evidence of knee osteoarthritis walk with different knee moments and muscle activity. *J Orthop Res*. 2017;35(8):1661-1670. doi:10.1002/jor.23465

217. Moreside J, Wong I, Rutherford D. Altered erector spinae activity and trunk motion occurs with moderate and severe unilateral hip OA. *J Orthop Res*. 2018;36(7):1826-1832. doi:10.1002/jor.23841

218. Bolink SAAN, Brunton LR, van Laarhoven S, et al. Frontal plane pelvic motion during gait captures hip osteoarthritis related disability. *HIP Int*. 2015;25(5):413-419. doi:10.5301/hipint.5000282

219. Watelain E, Dujardin F, Babier F, Dubois D, Allard P. Pelvic and lower limb compensatory actions of subjects in an early stage of hip osteoarthritis. *Arch Phys Med Rehabil*. 2001;82(12):1705-1711. doi:10.1053/apmr.2001.26812

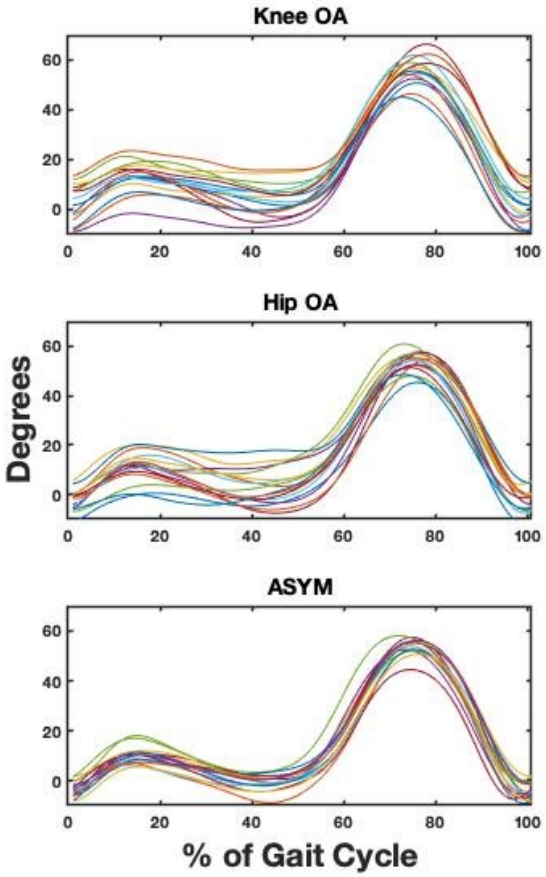
220. Charlton JM, Hatfield GL, Guenette JA, Hunt MA. Toe-in and toe-out walking require different lower limb neuromuscular patterns in people with knee osteoarthritis. *J Biomech*. 2018;76:112-118. doi:10.1016/j.jbiomech.2018.05.041

221. Harding GT, Hubley-Kozey CL, Dunbar MJ, Stanish WD, Astephen Wilson JL. Body mass index affects knee joint mechanics during gait differently with and without moderate knee osteoarthritis. *Osteoarthr Cartil*. 2012;20(11):1234-1242. doi:10.1016/j.joca.2012.08.004

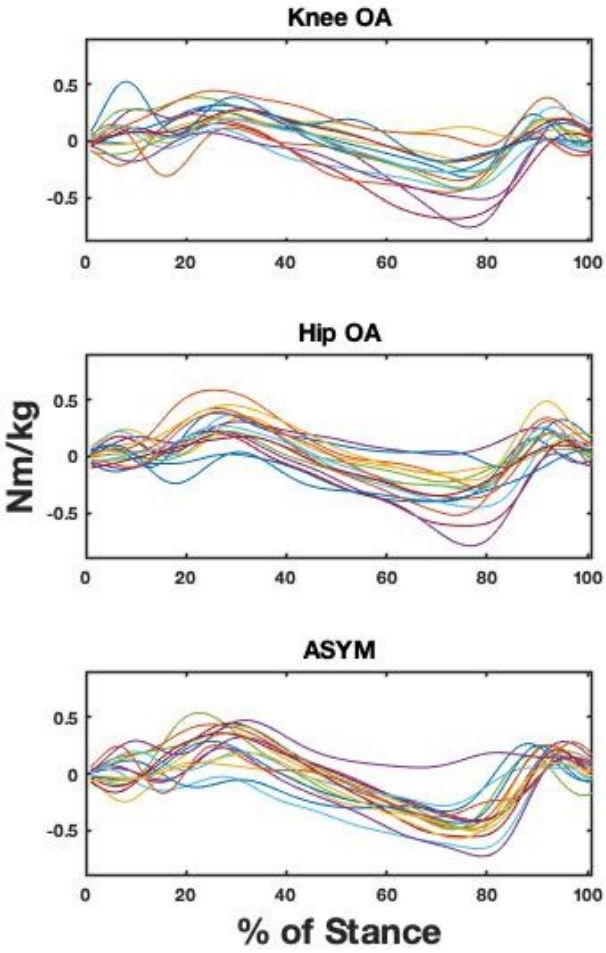
222. Lewek MD, Rudolph KS, Snyder-Mackler L. Quadriceps Femoris Muscle Weakness and Activation Failure in Patients with Knee Osteoarthritis. *J Orthop Res*. 2004;22(1):110-115. doi:10.1016/S0736-0266(03)00154-2.

223. Song JL, Hidler J. Biomechanics of overground vs. treadmill walking in healthy individuals. *J Appl Physiol*. 2008;104(3):747-755. doi:10.1152/japplphysiol.01380.2006

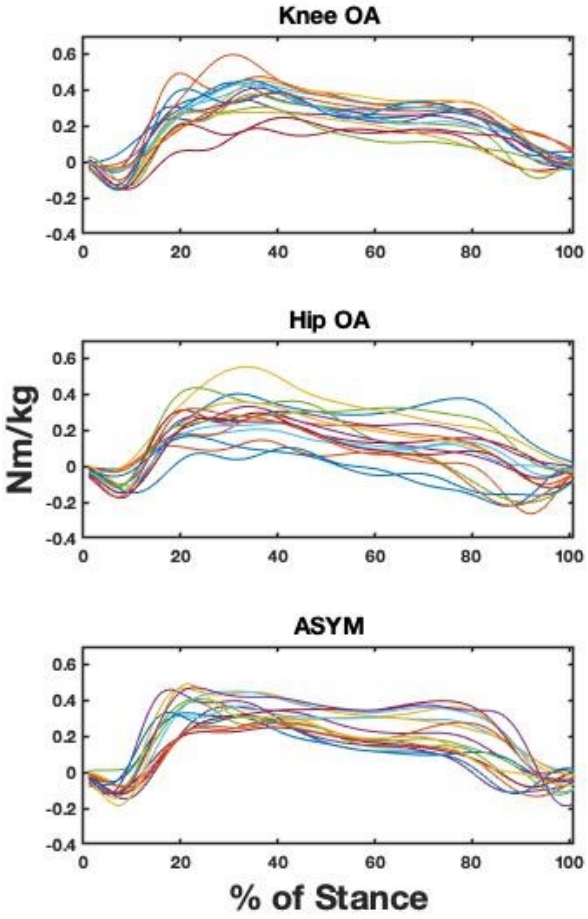
Appendix A: Group Waveforms & Group Average MVIC Normalized Muscle Activity



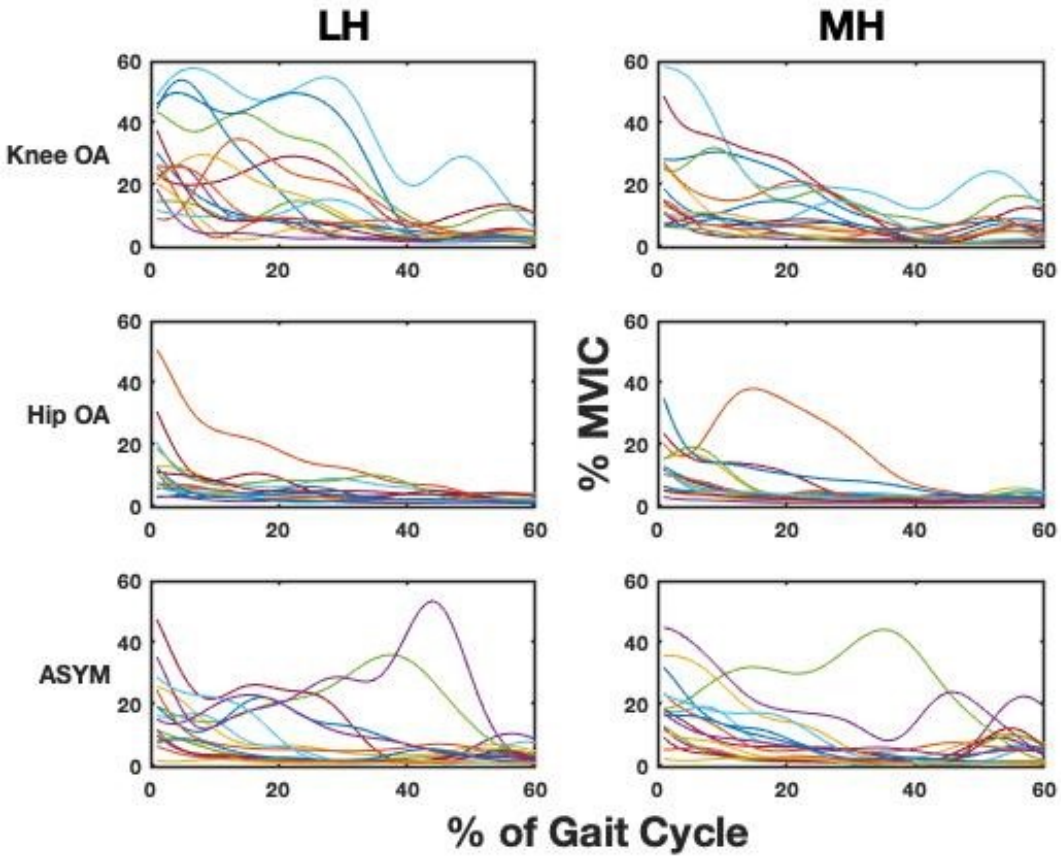
Supplementary Figure 1. Sagittal plane knee joint range of motion (degrees) throughout the gait cycle for knee OA, hip OA, and asymptomatic (ASYM) participants.



Supplementary Figure 2. Sagittal plane flexion-extension moment (Nm/kg) throughout the stance phase for knee OA, hip OA, and asymptomatic (ASYM) participants.



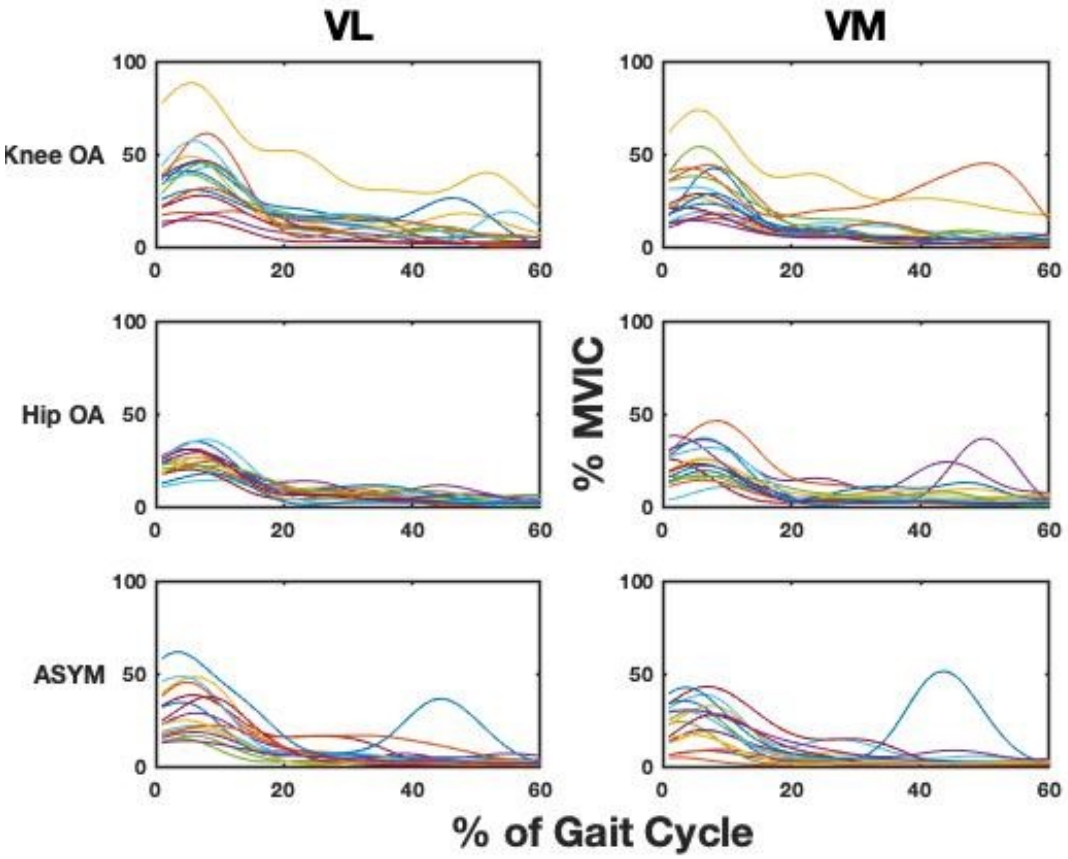
Supplementary Figure 3. Frontal plane knee adduction moments (Nm/kg) throughout the stance phase for knee OA, hip OA, and asymptomatic (ASYM) participants.



Supplementary Figure 4. Mean MVIC normalized lateral (LH) and medial (MH) hamstring amplitudes throughout stance phase for knee OA, hip OA, and asymptomatic (ASYM) participants.

Supplementary Table 1. Mean (Standard deviation) Group MVIC normalized activation amplitudes (%MVIC) for the lateral (LH) and medial (MH) hamstring muscles throughout the stance phase for knee OA, hip OA, and asymptomatic (ASYM) participants.

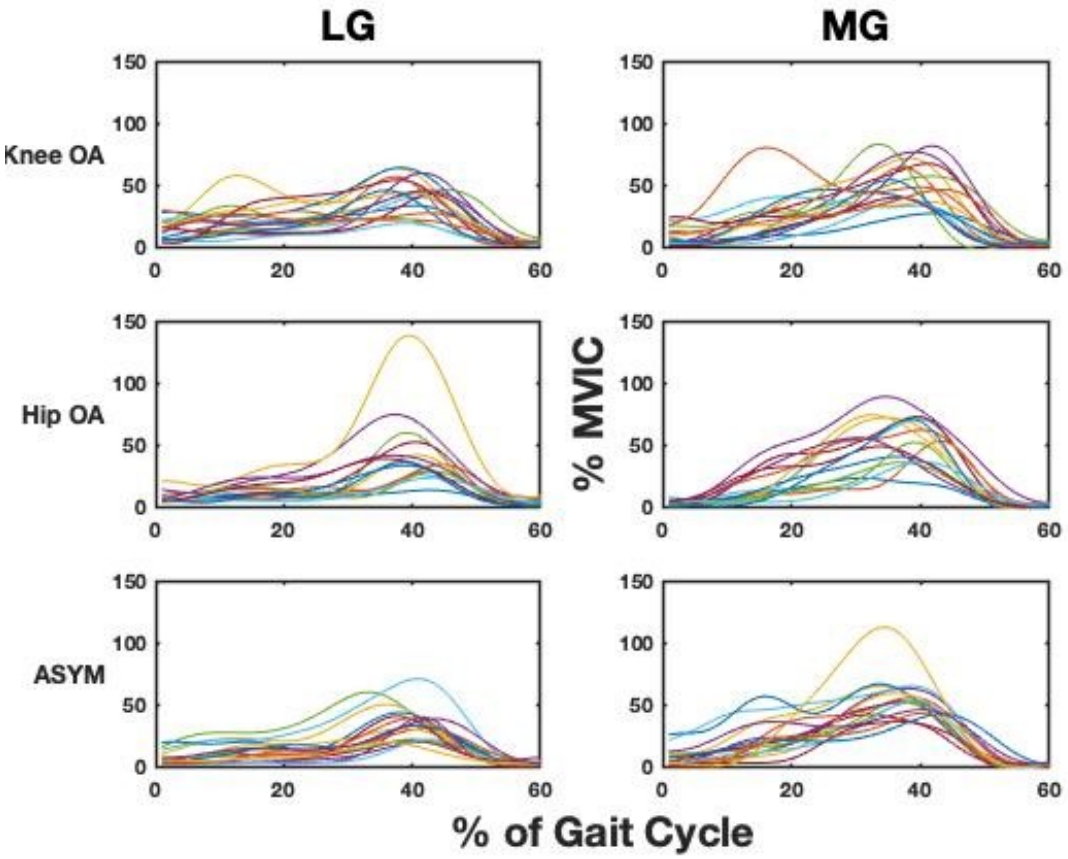
	Knee OA	**Hip OA**	**ASYM**
LH	13.3 (7.8)	4.5 (2.6)	7.3 (3.0)
MH	8.9 (4.5)	4.8 (2.8)	7.2 (2.7)



Supplementary Figure 5. Mean MVIC normalized lateral (VL) and medial (VM) quadriceps muscle amplitudes throughout stance phase for knee OA, hip OA, and asymptomatic (ASYM) participants.

Supplementary Table 2. Mean (Standard deviation) Group MVIC normalized activation amplitudes (%MVIC) for the vastus lateralis (VL) and vastus medialis (VM) muscles throughout the stance phase for knee OA, hip OA, and asymptomatic (ASYM) participants.

	Knee OA	**Hip OA**	**ASYM**
VL	16.7 (11.3)	9.5 (7.5)	11.6 (10.2)
VM	13.2 (8.4)	9.3 (7.0)	9.8 (8.4)



Supplementary Figure 6. Mean MVIC normalized lateral (LG) and medial (MG) gastrocnemii muscle amplitudes throughout stance phase for knee OA, hip OA, and asymptomatic (ASYM) participants.

Supplementary Table 3. Mean (Standard deviation) Group MVIC normalized activation amplitudes (%MVIC) for the lateral gastrocnemius (LG) and medial gastrocnemius (MG) muscles throughout the stance phase for knee OA, hip OA, and asymptomatic (ASYM) participant.

	Knee OA	**Hip OA**	**ASYM**
LG	22.9 (10.4)	11.6 (12.1)	18.0 (9.8)
MG	25.7 (15.6)	23.9 (18.2)	21.9 (14.4)