Lower Limb Biomechanics in Response to Unexpected Walking Surface Translations During Gait in Individuals with Knee Osteoarthritis: A Comparison Study to Healthy Asymptomatic Individuals

By

Felicia Licht

Submitted in fulfillment of the requirements

for the degree of the Master of Science

at

Dalhousie University

Halifax, Nova Scotia

August 2023

Dalhousie University is located in Mi'kma'ki, the

ancestral and unceded territory of the Mi'kmaq.

We are all Treaty people.

Table of Contents

List of Tables

List of Figures

Abstract

Knee osteoarthritis is a prevalent musculoskeletal condition affecting mobility and function. Walking surface perturbations unpredictably challenge individuals to test joint function. Thesis' objectives were to determine the response of the lower limb after experiencing a 3cm medial perturbation through the analysis of the support moment and leg stiffness. Thirty-five individuals with knee osteoarthritis and thirty-five older adults underwent a perturbation protocol using a dual-belt instrumented treadmill while data on knee motion and ground reaction forces were collected. Support moment outcomes demonstrated that both groups required more support to maintain walking in response to a 3 cm medial perturbation. Further, both groups utilized a reorganized control strategy with dominating ankle contribution. Leg stiffness outcomes supported that both groups required more leg stiffness to maintain stability with an increase in leg stiffness indicating an adjustment to increase functional performance. Overall, both groups responded to walking perturbations with similar lower extremity responses.

List of Abbreviations Used

OA – Osteoarthritis

OARSI – Osteoarthritis Research Society International

ASYM – Asymptomatic

ROM – Range of Motion

KAM – Knee Adduction Moment

MOA – Moderate Knee Osteoarthritis

WHO – World Health Organization

ICF - International Classification of Functioning, Disability and Health

vGRF – Vertical Ground Reaction Force

GRF –Ground Reaction Force

KFM – Knee Flexion Moment

WOMAC - Western Ontario and McMasters Universities Osteoarthritis Index

JAR – Joint Action Research

KOS-ADLS - Knee Outcome Survey Activities of Daily Living Scale

KOOS - Knee injury and Osteoarthritis Outcome Score

ASIS – Anterior Superior Iliac Spine

CMRR - Common Mode Rejection Ratio

A/D – Analog-to-Digital

N – Newtons

T0 – Ensemble Averages of Strides Pre-Perturbation

T1 – Ensemble Averages of Strides Post-Perturbation

MVIC – Maximum Voluntary Isometric Contraction

SPSS - IBM® SPSS® Statistics 27

Acknowledgements

There are several people I would like to thank for my experience throughout the Masters of Rehabilitation Research program in the School of Physiotherapy at Dalhousie University. I would like to thank my supervisor, Dr. Derek Rutherford for his never-ending enthusiasm, guidance, encouragement, and knowledge. His passion for research, curiosity, and dedication to higher education is inspiring and helped to motivate me throughout this process. He inspires his students to put their best foot forward while maintaining a supportive environment where mistakes are made and learned from. Thank you for making my Masters experience one of learning, but also one of excitement and joy.

I would also like to thank my committee members, Dr. Cheryl Kozey and Dr. Janie Wilson for your time, support, and insightful feedback that you both provided to this MSc work. Additionally, I would like to thank Dr. Stanish, Dr. Wong, and Dr. Urquhart for recruitment of individuals with knee OA, the participants for their time and effects in helping with this study, as well as Dr. Matt Baker and Mr. Chris Murphy for their assistance with data collection and processing.

Further, I would like to thank everyone I had the privilege of meeting from the Joint Action Research and Dynamic of Human Movements lab. Thank you all for the assistance, guidance, and most importantly, the banter and laughs.

Finally, I would like to thank my friends, family, and partner for being there through both the good and bad times. You all provided endless support, love, and motivation throughout this process which I will be forever grateful for.

Chapter 1 – Introduction

Osteoarthritis (OA) is a heterogenous disorder that is progressive in nature (4,5) and is shown to affect a large number of Canadians but is also prevalent worldwide (6–8). Specifically, OA is projected to effect 1 in 4 individuals over the next 30 years and is associated with a significant economic burden to those effected and the health care system (6,9). In Canada, it is estimated that OA currently accounts for $10 billion in direct health care cost, $17 billion in indirect health care cost and is predicted to reach $550 billion in direct and $909 billion in indirect costs by 2040 (6). As the only definitive treatment for OA is joint replacement surgery, research must be conducted in early disease stages to lower the burden of this disease.

The OA Research Society International (OARSI) has created a standard for the classification of OA to include components of anatomic, molecular, and physiologic disease elements with disease severity increasing when illness components are integrated (5,10). Knee OA is thought to initiate when joint tissues fail to repair at a molecular level (10–14). The degenerative cycle of OA continues as mechanical load applied to the joint exceeds the capacity of the injured joint tissue and OA progresses (10–14). Medial tibiofemoral knee OA is more prevalent compared to lateral compartment knee OA (15) because of asymmetrical joint loading during weight-bearing activities (16,17).

Individuals with knee OA commonly complain of physical limitations that effect activity levels due to buckling, shifting, or giving away of the knee while walking (18–20). These events further lead to inactivity due to a decrease in confidence because of associated feelings of instability (20–22). Feinglass et al. (23) showed that decreased levels of activity are in direct association with knee OA progression and reduce an individual's quality of life through a decrease in joint movement, an increase in fatigue and depression, a decreased pain tolerance and an increased risk in developing comorbidities (24,25). Compared to older adults who take an average of 6500 – 8000 steps a day (26,27), individuals with knee OA take significantly less steps at 5500 steps or less per day (26). Also, individuals with knee OA are found to walk with a slower self-selected speed (28–33). Therefore, movement and exercise should be promoted in a rehabilitation setting to preserve knee joint health at earlier stages of knee OA.

While individuals with knee OA show a decrease in physical abilities, changes to knee joint function have also been identified. Gait analyses are commonly used to study knee joint function between individuals with knee OA and an asymptomatic (ASYM) control group (34,35,44–47,36–43). During dynamic activities, such as walking, the goal is to achieve an equilibrium between stability and mobility. However, the equilibrium is broken in individuals with knee OA, and many individuals feel knee instability (4,42,48,49). Individuals with knee OA are challenged during loading and mid stance where the centre of mass has reached its furthest position over the supporting limb in the frontal plane and stability is entirely reliant on the supporting limb response (50,51). During the gait cycle, an overall decrease in the knee range of motion (ROM) in the sagittal plane is identified for individuals with knee OA (37,40,41,52–55) with a further decrease in ROM noted with increasing disease severity (56,57) and self-reported feelings of knee instability (40,54,55,58). In addition, a decrease in the difference between early external peak knee flexion moment and late peak knee extension moment (42,43,48,59) is thought to be indicative of a reduced ability to unload the joint during midstance (40,48). It has also been termed a “stiff knee” gait utilized by individuals with knee OA to attempt to stabilize the knee through stance phase (48,60,61). Finally, individuals with knee OA are commonly shown to walk with an increased knee adduction moment (KAM) (32,48,62,63) as increased loads are placed through the medial compartment of the knee joint (16,64).

While these analyses have provided an in depth understanding of the direct effect knee OA has on the knee joint, the effect of knee OA on the entirety of the lower limb should be taken into consideration. Compensations from the hip and ankle could occur during gait to overcome the effects of knee OA (65). Two measurements that have been used in gait analysis to characterize the integrated response of the lower limb include the support moment and leg stiffness.

The support moment is calculated as the sum of the net internal extension moments of the lower limb - the knee extension, hip extension and ankle plantar flexion moments - during stance phase (66–68). Conceptually, the support moment can be thought of as the net moment that prevents collapse during weight bearing activities and contributes to lower limb support (66–68). Comparing ASYM individuals to individuals with knee OA using gait analysis has identified that individuals with knee OA walk with a decreased support moment (69–71). Zeni and Higgins further noted that a significant change in the peak support moment was only noted at faster speeds beyond 1.0 m/s (69). While significant differences in the peak support moment were not found at all speeds between groups, the joint moment contributions to the support moment were significantly different between a group of individuals with knee OA vs. ASYM individuals (69) and further between individuals with knee OA and those self-reporting instability (71).

Overall, it was suggested that individuals with knee OA walk with a reorganized control strategy to maintain a similar support moment to reduce knee compression forces and joint loading (69).

Leg stiffness is another component used to quantify the effect of knee OA on the lower limb. Leg stiffness is measured as the ratio of peak vertical ground reaction force (vGRF) over the change in leg length during stance phase (72). Leg stiffness is commonly reported for tasks of hopping or jumping (73–76), normal walking (77), running (72), and with comparisons between individuals with knee OA and ASYM individuals (78–80). Wei et al. (78) identified that individuals with bilateral knee OA typically walk with an increased leg stiffness to prevent collapse while walking. They suggested that an increased overall leg stiffness was used to contribute to biomechanical stability when accepting body weight during single leg support (78). While this has been identified in individuals with bilateral knee OA, little to no research was found when studying individuals with unilateral knee OA using this metric.

Great strides are being made to classify knee OA in a controlled walking environment, as summarized above, however, a disconnect between reported results in movement arise when an individual moves into a real-world scenario where unpredictable walking conditions are present. Therefore, to study the affects of an unpredictable walking environment and the response of individuals with knee OA, perturbation studies have been conducted (49,81–87). Commonly used in perturbation studies is a dual-belt instrumented treadmill that can apply frontal plane surface translations at random occurrences unknown to the individual, helping to eliminate a preparatory response (88). Through an analysis of discrete knee joint motion and moment metrics, individuals with knee OA were not found to biomechanically alter their gait in response to a perturbation despite these individuals reporting issues with buckling of the knee joint when challenged (81,86,87). In addition, they demonstrated elevated and prolonged muscle activation patterns as a direct response to a perturbation greater than 2 cm (81,86,87) suggesting a stabilization pattern is used in response to a perturbation (81). While elevated and prolonged muscle activation patterns are noted in individuals with knee OA immediately following a walking surface perturbation, ASYM individuals responded in a similar manner (81,83,85,86). It is unclear why individuals with knee OA are not responding to a perturbation differently than ASYM individuals despite having knee OA. Additionally, further questions arise such as how individuals with knee OA respond to walking challenges and does this response involve a compensating mechanism from other lower limb joints such as the hip and/or ankle? Compensations in the lower limb may be occurring at the hip and/or ankle because of knee OA in response to the perturbation. These compensations are potentially being missed in previous investigations by isolating the analysis to knee joint biomechanics specifically. With these questions in mind, the focus of my thesis was to analyze the two metrics characterizing the lower limb – the support moment and leg stiffness –to further understand the response of the lower limb to a walking perturbation in individuals with knee OA.

1.1 Overall Objective

The main purpose of this study was to determine how individuals with moderate knee OA (MOA) and ASYM individuals respond to unexpected medial surface translations during gait.. This investigation looked to characterize the response in terms of the lower limb as a whole during the stride following the perturbation (response stride).

1.2 Specific Objectives

The specific objectives were:

1. To determine whether the peak support moment and percent contributions from the hip, knee, and ankle were altered with an unexpected 3 cm medial walking surface translation during stance for ASYM individuals and individuals with knee OA.
2. To perform an exploratory study to determine reference values for leg stiffness in individuals with knee OA and ASYM individuals using a dual-belt instrumented treadmill. Additionally, to determine whether leg stiffness was altered immediately after the application of an unexpected 3 cm medial walking surface translation during stance for individuals with knee OA compared to ASYM individuals.

1.3 Hypotheses

The hypotheses corresponding to objective 1 included:

a. Both individuals with knee OA and ASYM individuals will increase their peak support moment in response to the unexpected surface walking translation.
b. Individuals with knee OA will respond to the surface translation with percent contributions of the hip, knee, and ankle joints that act to decrease the knee percent contributions with an increase in hip percent contribution.

c. ASYM individuals will show no significant changes in percent joint moment contributions in response to the perturbation.

The hypotheses corresponding to objective 2 included:

a. The leg stiffness calculation will produce comparable values between baseline and strides pre-perturbation that are not significantly different.
b. Both individuals with knee OA and ASYM individuals will increase their leg stiffness in response to an unexpected 3cm medial surface translation.
c. Individuals with knee OA will have a lower leg stiffness compared to ASYM individuals.

Chapter 2 – Review of Relevant Literature

2.1 Osteoarthritis

2.1.1 What is Osteoarthritis

OA is a heterogenous disorder that entails the progressive loss of articular cartilage, subchondral cysts, osteophyte formation, muscle weakness and possible synovial inflammation with varying degrees of severity (4,5). OA is prevalently seen in aging populations as degradation of joints occur throughout one's lifespan, but OA is not a direct result of aging (89). Joint health can be thought of as an equilibrium process between joint tissue repair and breakdown. If this equilibrium is broken and the mechanical load applied to the joint exceeds the joint tissue capacity, then OA can occur due to the failed repair of joint tissue at a molecular level (10–14). Commonly noted risk factors of OA include joint injury, obesity, genetics, and anatomical factors that affect joint mechanics (4,11,89).

2.1.2 Classification of Osteoarthritis

OA severity was first characterized by Kellgren and Lawrence (90) using x-ray imaging to distinguish key osteoarthritic changes. They developed the Kellgren and Lawrence scale which classified OA from Grades I-IV and progressed in severity from doubtful joint space narrowing to the most severe case of OA being no visible joint space, osteophyte formation, subchondral hardening, cyst formation, and deformity of bone endings (90). While this scale was accepted by the World Health Organization (WHO) in 1961 (91,92), researchers have found the application of the scale to be inconsistent (93–

95). In addition to inconsistencies using the Kellgren and Lawrence scale, Felson et al. has questioned the importance of radiographic disease classifications when these findings do not always correlate with symptomatic responses (14,93) which has put into question how OA should be classified as a disease.

OARSI has sought to develop a standardized definition of OA classification using principals of both disease and illness (5,10). Disease refers to abnormalities of structure and function that can be scientifically identified, whereas illness refers to the human response to the disease (5,10). While disease can be more readily defined with objective measures, illness is harder to classify due to varying subjective measurements such as pain (96), instability (21,97) and physical limitations (19) which are commonly reported by patients with OA. It has been found that disease and illness features of OA are poorly correlated (5,98,99), emphasizing the importance of both features in the classification of the disorder. OARSI has overall suggested OA be characterized to include anatomic, molecular and physiologic disease elements with the severity of OA increasing as an individual transitions from disease to illness (10).

While research in OA continues to evolve and become more fluid in treatment options, the only definitive treatment for OA is a total joint replacement. With large wait times exceeding acceptable benchmarks for joint replacement surgeries, therapeutic interventions focused on disease management and pain reduction should be a health care provider’s focus (11). To reduce total knee replacement surgeries, research is being done in both early and moderate stages of OA in attempts to slow disease progression and reduce total joint replacement needs.

2.1.3 Economic Burden

OA is a debilitating disease that can negatively impact an individual's quality of life and causes a large economic burden to the individual and health care system. In 2011, the Arthritis Alliance of Canada estimated OA would effect 1 in 4 individuals over the next 30 years, with knee OA proving to be extremely problematic as it drastically affects individual’s lives as well as the health case system (6). One in three workers of the employed labor force have reported difficulty working due to OA (6). Individuals with debilitating OA thus take on a personal economic cost resulting from a loss in income, and out of pocket expenses for medical treatment (9,100). These personal expenses have previously been estimated to total annual costs of $12 000 in 2002 (9) and has certainly increased since. Additionally, personal costs to an individual suffering from OA was positively correlated with disease severity (9). Finally, among an increase in personal expenses, individuals suffering from OA report greater levels of depression, stress, role conflict, and behavioural coping with increased disease severity (101) which leads to a decrease in quality of life.

In Canada, between 2019-2020, there has been a 17.1 % increase in knee replacements done over the last five-year period. Nova Scotia saw a 23.9 % increase in knee replacements due to our statistically older population (8), with OA resulting in 99 % of the diagnosis for knee joint replacements (7,8). A decrease in knee replacements performed was seen from 2020 to 2021 due to the COVID-19 pandemic and resulting lack in elective surgeries performed (7). Although this statistic has decreased, it is not from a lack of need. More than ever we are now struggling to reach national benchmark wait times for knee joint replacement surgeries as a result of the COVID-19 pandemic

(7). In addition to the initial need for a total joint replacement, revision surgeries encompass approximately 7 % of total knee replacements performed and are associated with a larger economic burden totaling $1.4 billion in expenses for surgeries alone (7,8,102). Overall, the Arthritis Alliance of Canada has estimated that OA currently accounts for $10 billion in direct health care cost and $17 billion in indirect health care cost and is predicted to reach $550 billion in direct and $909 billion in indirect costs by 2040 (6). To prevent further financial burden from total knee joint replacements, improvements need to be made in both early and moderate stages of knee 0OA.

2.1.4 Physical Activity and Limitations

The WHO worked to develop a standardized classification of the functioning and disability associated with health conditions and in turn distributed the International Classification of Functioning, Disability and Health (ICF) (103). The ICF model is intended for users to classify a disease in terms of body functions and structures leading to impairment, activity limitations, and participation restrictions with the addition of these three factors being influenced by both environmental and personal factors (103) (Figure 2.1).

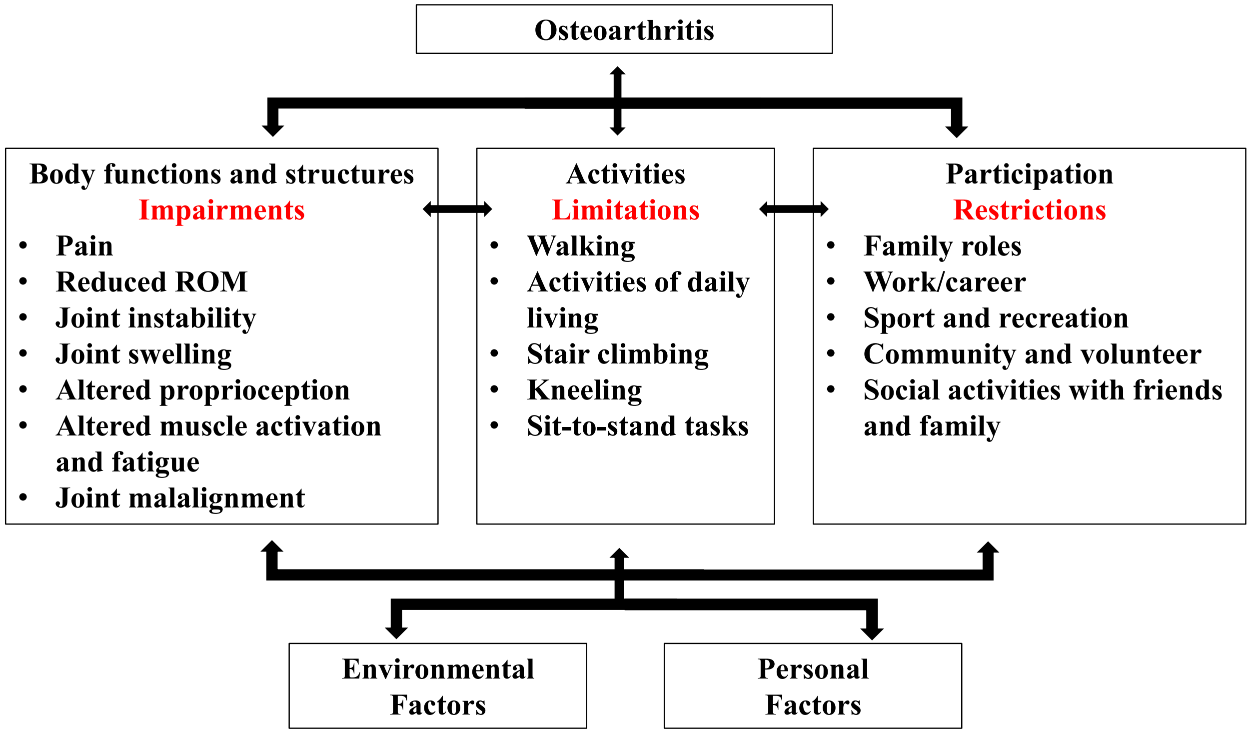

Figure 2.1: The ICF model adapted to represent OA. Modified from Dreinhofer et al. (1).

A comprehensive ICF core set for OA was identified with 144 categories on body functions, 49 on body structures, 165 on activities and participation and 43 on environmental factors (1). This indicates that activity limitation and participation are significant measures to take into consideration when managing patients with OA.

A common complaint (63 % of individuals as reported by Fitzgerald et al.) affecting activity levels in individuals with knee OA is knee buckling during walking (18–20) and other tasks. This in turn leads to a decrease in confidence due to feelings of knee instability (20–22). As a result of a decrease in confidence, individuals with knee OA further demonstrate reduced levels of activity and functional limitations (23) whereby 44 % of individuals confirm that instability affects their ability to function (20). Decreased levels of activity are directly associated with knee OA progression and a reduction in quality of life through a decrease in joint movement, an increase in fatigue and depression, a decreased pain tolerance and an increased risk in developing comorbidities (23–25). Although physical activity is decreased in individuals with knee OA, moderate to vigorous activity has not been shown to cause further damage to the knee joint and has a large benefit on an individual's quality of life (23,24). King et al. assessed the relationship of hip and knee OA to walking difficulty in conjunction with other co-morbidities (104), and they identified that walking disability probability increased from 5 – 10 % to 40 % if an individual has OA and up to 60 – 70 % if an individual has OA as well as diabetes mellitus and cardiovascular disease (104). The greatest independent contributor to this increased probability of walking disability was contributed to OA and they concluded that OA management may be a higher priority than vigorous management of other conditions in maintain walking mobility (104). Therefore, movement and exercise should be promoted in a rehabilitation setting to preserve knee joint health at earlier stages of knee OA. Rehabilitation measures should be tailored to individuals to address their self-reported conception of instability to promote safe activity and bolster confidence in motion.

2.1.5 Joint Stability Adaptations

At a mechanical level, Panjabi's framework of joint stability has been used to understand how neural, skeletal, and muscular systems work together and adapt when disease occurs (2). Panjabi suggests that stability of a joint is satisfied through three subsystems: 1) the passive subsystem composed of bones and ligaments, which provide stability through motion; 2) the active subsystem composed of muscles and tendons, which acts to generate force to provide stability; 3) the neural subsystem composed of nerves and central nervous system (Figure 2.2), which receives neural information and determines the required processes needed to maintain stability– all three of which are functionally interdependent (2).

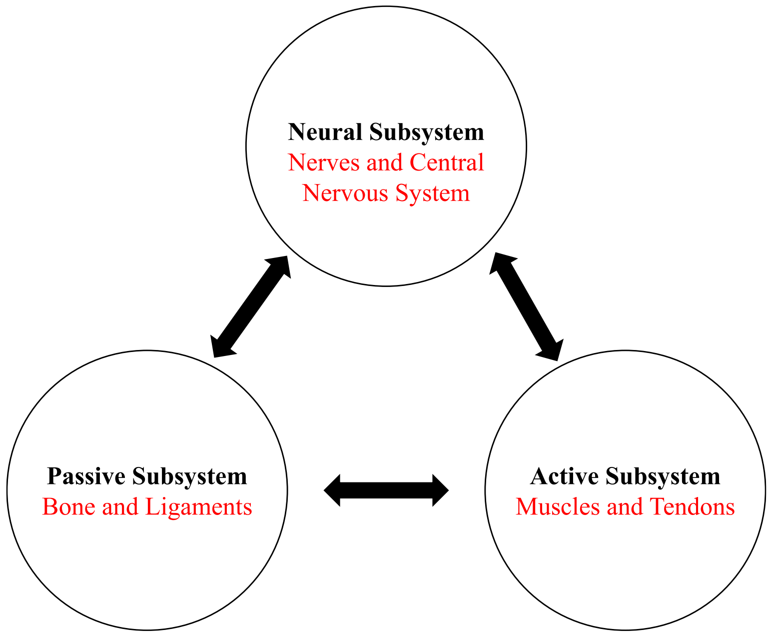

Figure 2.2: Panjabi's framework of joint stability. Modified from Panjabi et al. (2).

When injury or malfunction occurs in one subsystem, the others must adapt to maintain stability through an immediate response, or a long-term adaptation response occurs (2). For example, if injury occurs in the passive subsystem, the neural subsystem will attempt to modulate the active subsystem to regain joint stability. If stability is not regained within these subsystems, an overall disfunction of the joint is noted, pain occurs (2), and limitations in physical activity occur as mentioned above. While the goal is to maintain joint stability, by adapting the 3 subsystems in ways such as altered joint kinematics, muscle activation, and loading patterns, this can have a detrimental effect on the knee joint and lead to further OA progression (40,55,60). To study these biomechanical adaptations noted in individuals with knee OA, gait analysis is readily used.

2.2 Gait Biomechanics

2.2.1 Gait Cycle

As noted, knee OA can severely affect individual's physical abilities. One common form of movement affected by knee OA is walking. To study walking habits in a person, parameters must first be standardized into a unit of measurement. The gait cycle (Figure 2.3) is a fundamental unit used to characterize walking and is identified as one cyclic repetition of both stance and swing by one limb (3,50,51). The gait cycle begins at initial contact (0 % of the gait cycle) and is completed when the ipsilateral foot strikes the ground (100 % of the gait cycle) – this is equal to one stride (3,50,51).

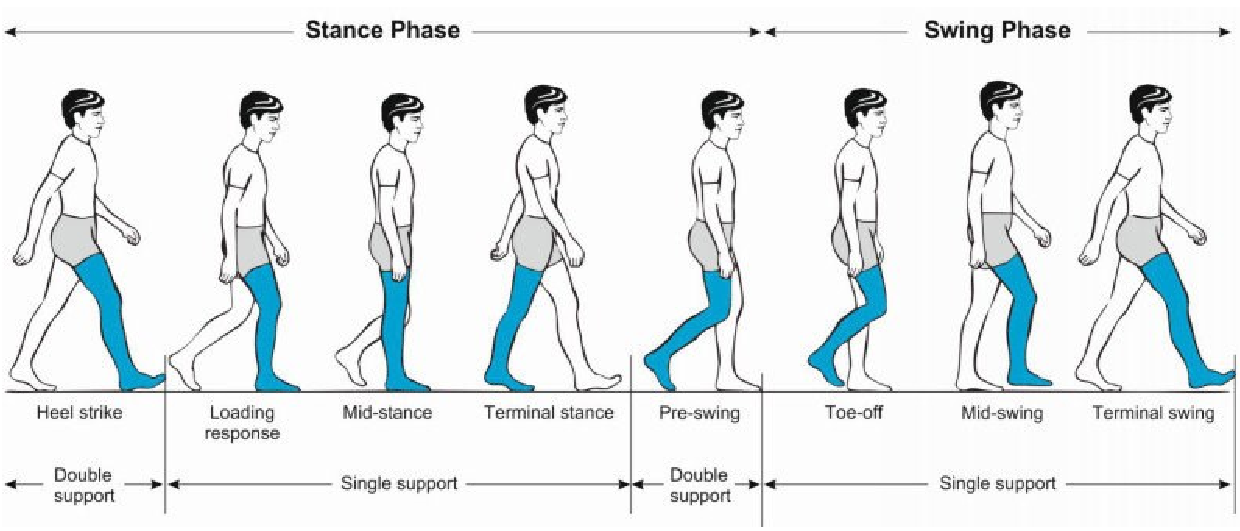

Figure 2.3: The gait cycle of the right leg split into the stance and swing phase. Obtained from W. Pirker and R Katzenschlager with open access under the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/) (3).

The gait cycle can be further broken into subcomponents consisting of stance phase and swing phase. Stance phase encompasses approximately 60 % of the gait cycle and is initiated at initial contact of the study limb to toe off while swing phase encompasses the remaining 40 % and is initiated at toe off of the study limb and ends with initial contact to complete the gait cycle (3,50,51). Double-limb support occurs when a person is transferring their weight from one limb to another and acts as the connection between stance and swing phase (50,51). Double-limb support is dependent on gait speed – as gait speed increases, the amount of time spent in double-limb support decreases and vice versa (50,51).

Mid stance is most commonly defined as the moment where the body's mass passes directly over the supporting lower extremity and occurs at roughly 30 % of the gait cycle or 50 % of stance phase (50,51). During mid stance, the centre of mass has reached its furthest anterior position over the supporting limb and stability is entirely reliant on the response of the supporting limb (50,51). If the supporting limb is unstable, as seen in individuals with knee OA, this leaves the effected limb vulnerable to collapse. By better understanding the response of the entire lower limb at mid stance, improvements in stability could be identified for people suffering from knee OA.

The knee joint kinematic pattern in the sagittal plane plays a vital role in the gait cycle. Specifically, if knee joint extension is limited, a functionally shorter leg results in a "crouched" position with compensatory motions seen in the hip and ankle to maintain stability (50,65). An uneven functional leg length as a result of a decreased knee ROM also leads to excessive trunk and centre of motion movement, all of which increases metabolic demands of walking (50). Therefore, compensation strategies are present to maintain gait fluidity, which incentivises the need to examine the entirety of the lower limb in response to knee OA.

2.2.2 Knee OA Kinematics

Through gait analysis, individuals with knee OA have consistently been shown to walk with altered kinematics, kinetics, and muscle activation patterns. Three-dimensional motion capture can be used to study joint movements (kinematics) and joint moments can further be computed through inverse dynamics using inertial properties, kinematics, ground reaction forces (GRF), and subject specific anthropometrics. Knee joint movements and moments are typically studied in the sagittal and frontal planes.

When comparing individuals with knee OA to ASYM individuals, contradictory differences in knee flexion angle at initial contact have been identified. Some studies have found individuals with knee OA walk with an increase in knee flexion angle at initial contact (40,41,44–47), while others have identified individuals with knee OA strike the ground with smaller knee flexion angles (105,106). While there are identified disparities amongst various groups, an increase in knee flexion angle at initial contact is more readily reported. A larger increase in knee flexion angle at initial contact is also identified with increasing radiographic knee OA severity (46,57). An influence of self-reported flares in knee pain has also been found to increase the initial knee flexion angle (45). It has been hypothesized that greater knee flexion angles are associated with higher sagittal plane loads placed on the knee during walking (107). In addition, individuals with knee OA have also demonstrated a decreased peak knee flexion angle prior to mid stance (40–43). Although these metrics are important waveform features, limitations arise when using a single point in a gait waveform due to methodology. A reduced reliability has been noted when comparing a single point which makes it harder to compare knee flexion values between groups, but a higher reliability is found when comparing ROM (88,108–110).

Through the gait cycle, an overall decrease in knee ROM during both stance and swing phases are identified for individuals with knee OA compared to an ASYM individuals (37,40,41,52–55) with a further decrease in ROM noted with increasing severity (56,57). It has been hypothesized that a decrease in knee ROM causes further joint damage and results in a sensation of pain (111,112). By not moving through full ROM, it is thought that a lack of extension during initial contact and loading response is transferring force to cartilaginous areas that are not suited for load bearing (111,112). In addition, individuals with self-reported knee instability while walking demonstrated a more reduced ROM during the loading response phase of the gait cycle which is thought to act as a compensatory strategy to regain stability (40,54,55,58). While this strategy could be used, active muscle engagement is needed and could fail an individual should they become fatigued or miss a cue for activation. Therefore, this is potentially not a consistent compensatory strategy. Overall, individuals with knee OA are walking with a reduced ROM to regain stability, but the change in sagittal plane ROM is negatively affecting joint integrity, which could lead to further degradation.

Frontal plane knee kinematics have also been investigated in individuals with knee OA, but to a lesser extent. It has been found that individuals with knee OA walk with increased frontal plane knee varus angles during stance phase when compared to ASYM individuals (34–39). This is thought to be a result of medial joint space narrowing and an opening of the lateral compartment (34). This increase in frontal plane angles is also seen with increasing OA severity (106). Varus thrust – the lateral bowing of the knee during gait – was also identified in individuals with knee OA in correlation with greater peak varus angles (36,96,113). Varus thrust is used as a visual movement to indicate misalignment of the knee joint with greater loads being placed on the medial compartment and is associate with knee OA disease progression (36,113) While these findings are consistent within the literature, the degree of difference should be taken into consideration as the accuracy of skin mounted maker placement when measuring bone movement influences measured joint angles and can result in seemingly larger frontal plane angles (34,114–116). Frontal plane kinematics have also demonstrated low reliability in individuals with knee OA (109), and so consideration should be taken when interpreting frontal plane movements.

2.2.3 Knee OA Kinetics

Kinetics studies the forces associated with movement. Joint moments are calculated using inverse dynamics, requiring GRF, kinematics, subject anthropometrics, and inertial properties. Moments can be used to examine internal and external forces delivered by muscles, ligaments and bony tissues resulting in movement (117,118). Through gait analysis, individuals with knee OA have demonstrated reduced peak vGRFs relative to body weight (34,40,80,105,118). While measured GRFs have shown variability within the literature it has been thought that this is likely due to variability in self-selected walking speeds within individuals with knee OA (40,119).

Within the gait cycle, the GRF creates an external knee flexion moment (KFM) during the loading response phase of gait as it is acting in a upward and posterior direction relative to the knee (118). Moving from midstance to terminal stance phase, the GRF shifts to create an external extension moment as it is now acting in a upward and anterior direction (118). In the sagittal plane, conflicting peak KFM results have been found in individuals with knee OA compared to ASYM individuals. Some groups have reported that individuals with knee OA walk with a decreased peak external KFM (32,42,43,59) whereas, others have reported an increased peak external KFM (118,120,121) with a further increase with greater OA severity (32,48). The variation in KFM is seemingly determined by quadricep strength of individuals with knee OA(42,59,118,121). When a decrease in peak external KFM is observed, the literature suggests that the lack of quadricep activity is due to a pain avoidance gait pattern to minimize knee joint loading (42,59). An increase in the peak external KFM is indicative of increased and continued quadricep contraction in an attempt to stabilize the knee joint (118,121). While there are conflicting results when measuring the KFM, it has been found that the KFM is substantially influenced by knee joint pain (122–125) and gait speed (34,59,80,126), which could additionally explain this variation in the literature. In addition, the knee sagittal plane moment outcomes have only shown good (approximately 0.60) intraclass correlation coefficients indicating variable reliability in the peak value measurements (88).

To better characterize the sagittal plane moments, the sagittal plane external flexion-extension dynamic moment has been reported (42,43,47,48,52,56,59). Most commonly, a decrease in the external flexion-extension dynamic moment is seen in individuals with knee OA and is defined as a combination of a decreased peak external flexion moment and a decreased peak external extension moment at terminal stance (42,43,47,48,52,56,59). Alterations noted in the sagittal plane dynamic moment in individuals with knee OA is thought to be indicative of a reduced ability to unload the joint during midstance (40,48). It has also been termed a "stiff knee" gait within the literature and is thought to be a mechanism that attempts to stabilize the knee through stance phase (48,60,61). While a stiff knee gait may act to stabilize an individual while walking, it has also been thought to lead to further knee joint degradation due to altered loading while walking (40,55,60).

More consistently reported is the KAM which is used to characterize loading distribution between the medial and lateral compartment of the knee (16**.** A higher external KAM would indicate an individual is loading the medial compartment more than the lateral compartment and is associated with a varus deformity (64). Individuals with knee OA have demonstrated greater peak external KAMs and KAM impulses compared to ASYM individuals (32,48,62,63). It is clear within the literature that individuals with knee OA are indeed walking with altered gait biomechanics.

These studies have provided an in depth understanding of the response of the effected knee joint during gait analysis in individuals suffering from knee OA but are limited in understanding the response of the lower limb as a whole and potential compensatory strategies that may be used to maintain stability. Two measurements that characterize the lower limb and can be utilized to explore knee OA influences on gait biomechanics are the support moment and leg stiffness. The support moment provides us with the opportunity to study the relationships among the ankle, knee, and hip during walking to determine whether compensatory strategies are occurring at other joints in individuals with knee OA. Consistent with combining joint moments to create the support moment, combined vGRFs and leg length can be used to calculate leg stiffness to characterize the effect of knee OA on the lower limb.

2.3 Support Moment

2.3.1 Hip and Ankle Moments in Individuals with Knee OA

While most literature focuses on biomechanical changes at the knee in individuals with knee OA, changes are also identified within the entire lower limb to maintain stability. During gate analysis, focusing on the sagittal plane moments, individuals with knee OA consistently demonstrated decreased external hip flexion moments during single leg stance compared to ASYM individuals (31,43,70,127). A reduced external hip flexion moment has been suggested to contribute to higher impact loading at initial contact (31). The external hip extension moment has shown some variability in results where some groups have found an increase in the internal hip extension moment (127) and others have found a decrease in the external hip extension moment (43). Huang et al. (127) has suggested that an increase in the internal hip extension moment could aid in lower limb stabilization during weight transfer. Further, when separating individuals with knee OA into groups by severity, Astephen et al. identified that individuals with severe OA demonstrated an increase in the external hip flexion moment during stance compared to both individuals with moderate knee OA and ASYM individuals (32,43).

In addition to the hip, biomechanical changes in the ankle have also been identified in individuals with knee OA. Most readily found in the literature, individuals with knee OA were found to also walk with reduced external plantar flexion moments (31,43,70,127,128). Again, individuals with severe knee OA showed alternate changes of a greater external ankle dorsiflexion moment during early stance and a smaller external dorsiflexion moment during later stance compared to ASYM individuals (32). With varying changes and discrepancies in biomechanical changes within knee OA, classifying the disease and progression can be difficult.

While changes in moments are identified for each joint of the lower limb, these measures have been shown to be sensitive to individual metrics and experimental technique (129). Goldberg and Stanhope have identified that all joint moments showed a significant interaction effect to walking speed and body weight (129) with an increase in variability at slower speeds (130). Zeni and Higgins further confirmed this interdependence in individuals with knee OA (69). While this interdependence is observed when looking at individual joint moments, the support moment measurement has not been found to have a similar interdependence to walking speed and body weight (66,69,130) which gives it the potential to be a more reliable metric in biomechanical analysis.

2.3.2 Support Moment

Joint moments are representative of the net affect of all muscle activity and are used to represent neural control acting at a joint (66). A net joint moment during walking is the summation of the hip, knee and ankle internal joint moments and is normalized to stance phase (66,67,69). Internal extension moments during stance phase are positive and flexion moments are negative (130). The support moment during stance phase is therefore the sum of the knee extension, hip extension, and ankle plantar flexion net internal moments (66–68) (Equation 1). This equation requires that these net internal moments are positive.

$$Support\ Moment = M_{Knee\ Extension} + M_{Hip\ Extension} + M_{Ankle\ Plantar\ Flexion} \qquad (1)$$

Conceptually, the support moment can be thought of as the net moment that prevents collapse during weight bearing activities and contributes to lower limb support (66–68). By investigating the support moment during single-leg stance, more information can be gathered on how one joint might be compensating for a lack of support from another joint (66,69), which can be evident in individuals with knee OA. This investigation can also provide insight to classify a stabilizing strategy in terms of the support moment as individuals with knee OA do not demonstrate consistent patterns in individual joint moments.

Comparing ASYM individuals to individuals with knee OA using gait analysis, it has been found that individuals with knee OA walk with a decreased support moment (69–71). Zeni and Higgins further examined the support moment at various speeds (69). They identified that there were no significant change in peak support moment at a controlled and self-selected walking speed, but a significant decrease was noted at faster walking speeds (69). With that being said, they additionally identified that while the support moment magnitude did not change, joint moment contributions to the support moment were altered (69). Individuals with knee OA were shown to reduce knee joint contributions at controlled and self-selected walking speeds and demonstrated an increase in ankle contribution and decrease in hip contribution when walking speed was increased (69). While these changes were present, individual walking speeds were not significantly related to joint contributions suggesting that joint contributions are dependent on the individual's control strategy while walking (69). Zeni and Higgins further suggested that individuals with knee OA walk with a reorganized control strategy to maintain a similar support moment by reducing the external knee flexion moment at all walking speeds to reduce knee compression forces and joint loading (69).

Comparing a cohort of individuals with knee OA and self-reported instability to those without self-reported instability has also led to differences in the support moment. Individuals with knee OA and self-reported instability have been shown to walk with a smaller support moment due to reduced contributions from the hip and ankle moment, but had increased knee moment contributions (71). Again, these findings indicate that individuals with knee OA and self-reported instability alter their walking biomechanics to maintain stability (71).

2.4 Stiffness

2.4.1 Knee Joint Stiffness

Stiffness is defined as the extent to which an object resists deformation in response to an applied force (131). In the literature, knee joint stiffness has both been computed (53,132) and identified as a change in the sagittal plane moment to represent a stiff knee gait (133). For example, Dixon et al. have calculated walking knee stiffness as the change in the sagittal plan joint angle in response to an applied joint moment from peak flexion to peak weight acceptance (53) whereas Hubley-Kozey et al. have identified a pattern in the external KFM to infer a stiff knee gait (133).

In relation to knee OA, individuals suffering from this disorder have generally been found to walk with an increase in knee joint stiffness (53,79,132–134). As mentioned, knee OA affects a person’s gait biomechanics and has been shown to lead to fall risk. Individuals who reported feelings of instability specifically demonstrated a lower knee joint stiffness compared to a subgroup of individuals with knee OA who did not report feeling unstable in their walking (79). This leads to the conclusion that feelings of instability while walking is associated with an increase in knee motion variability (135) that negatively affects lower limb control. Zeni et al. (134) suggests that in individuals with knee OA, an increase in knee joint stiffness is used as a compensatory walking strategy to attempt to increase stability. In addition to an increase in knee joint stiffness, individuals with knee OA were found to walk with a decrease in sagittal plane knee motion (40,53,80) which was shown to significantly decrease the likelihood of falling (135,136). While others identify neurological changes as a reason for an increase in knee joint stiffness (37), it is believed that changes in joint biomechanics are responsible for the increase in knee joint stiffness during walking (53,134,137). This is supported through the correlation between knee joint stiffness and decreased sagittal plane knee motion (135).

Prior to biomechanical investigations of knee stiffness, the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC) was, and is still used, to classify knee stiffness (53). Dixon et al. (53) found that while walking knee stiffness construct validity is supported, there is a poor correlation between measured walking stiffness and that reported using the WOMAC. In their study, knee stiffness was calculated during walking and showed an increase in knee stiffness that corresponded to a decrease in sagittal plane knee motion due to greater knee flexion at initial contact (53). Their study produced a high test-retest reliability with an intraclass correlation coefficient of 0.95 (53). Although an increase in knee joint stiffness was demonstrated, poor correlation was present between measured knee stiffness and self-reported stiffness using the WOMAC

(53). Overall, it was concluded that use of the WOMAC on its own will not detect the degree of stiffness and its overall effect on function and biomechanical measurements of knee joint stiffness should be used to identify significant changes in function (53).

When comparing differences in knee joint stiffness between the symptomatic and ASYM limbs, it has been found that individuals with knee OA have a significantly greater knee joint stiffness in their symptomatic knee while walking (132). Surprisingly, no significant findings were identified when comparing the walking time effects on knee joint stiffness (132). This could indicate that while individuals with knee OA do experience an increase in knee joint stiffness, it is a learned compensatory walking strategy to maintain stability as previously suggested (134).

Finally, when examining other features of walking compared to knee joint stiffness, the speed of walking was shown to increase measured knee joint stiffness in individuals with moderate knee OA, individuals with severe knee OA and ASYM individuals (134). While increasing walking speed has a global increase on knee joint stiffness among groups, individuals with severe knee OA showed a significant increase in knee joint stiffness compared to the other two groups at both a self-selected and increased walking speed (134). This indicates that with an increase in knee OA severity, there is also an increase in knee joint stiffness. While knee joint stiffness is useful in characterizing a compensatory strategy used by individuals with knee OA, it is limited to specific testing methodologies. Therefore, leg stiffness computation could aid in the examination of the lower limb response while decreasing methodology discrepancies.

2.4.2 Leg Stiffness

Commonly, knee OA literature is specifically focused on the direct effect to the knee joint, but rarely relates findings to a larger picture of how knee OA is affecting the entire lower limb. Joint stiffness is more commonly reported than an overall leg stiffness and there are conflicting opinions over the relationship between joint stiffness and leg stiffness whereby some have shown that leg stiffness is not determined by joint stiffness (77) and others believe individual joint stiffness directly influences leg stiffness (79). It is observed in clinical practice that compensatory affects are seen by other joints to overcome knee OA effects (65). Leg stiffness can be used to study the effects of knee OA on the whole lower limb opposed to solely the knee joint and can be thought to represent the control of the musculoskeletal system on the lower limb (78). Within this definition, leg stiffness can be maintained by an increase in the skeletal component by decreasing the flexion of the lower limb joints, or by increasing the muscular component by increasing muscle activity and resulting joint moments (78).

Leg stiffness is measured as the ratio of peak vertical ground reaction force over the change in leg length during stance phase (72) (Appendix B). Leg stiffness (K_{leg}) is calculated using equation 2 where F_{max} is the peak vGRF (N) normalized to body weight (N), l_o is the leg length at initial contact (m) and l_{min} is the minimum leg length (m) through stance (72).

$$Kleg = \frac{\text{Fmax}}{(\text{lo} - \text{lmin})/\text{lo}} \qquad (2)$$

Leg length can be calculated by extracting motion capture data from proximal (i.e., pelvis markers) and distal (i.e., center of pressure or calcaneus marker) locations measured in the X, Y and Z coordinate system. A vector is then created between the proximal and distal locations and the magnitude of the vector is used to represent the changing leg length through the gait cycle (Figure B.2).

In the literature, leg stiffness is commonly reported for tasks of hopping or jumping (73–76), normal walking (77), running (72), and with comparisons between individuals with knee OA and ASYM individuals (78–80). Lower extremity stiffness has also been investigated as a tool for performance training and injury prevention whereby it is thought that leg stiffness can be modified and used as a part of training intervention programs (138). Leg stiffness computation methodology should also be taken into consideration when comparing direct values between studies as this measurement has been shown to differ depending on the data collection processes and computation of leg stiffness (139–141). While these discrepancies exist, making comparisons within the same study should produce comparable values.

Wei et al., (78) found that individuals with bilateral knee OA typically walks with an increased leg stiffness to prevent collapsing while walking. Leg stiffness was calculated in a similar way as above whereby leg stiffness was measured as the change in vGRF compared to the change in leg length (78). They suggested that an increased overall leg stiffness was used to contribute to biomechanical stability when accepting body weight during single leg support (78). Similarly to knee joint stiffness, an increase in leg stiffness also corresponded with a decrease in sagittal plane external knee moments via reduced knee flexion at initial contact (78). Wei et al. also found that by increasing overall leg stiffness, individuals with knee OA reduced their muscular demands through this compensatory strategy (78). In individuals with bilateral knee OA, they determined that an increase in leg stiffness was mainly achieved by increasing the joint stiffness at the knee with minimal changes to hip and ankle stiffness (78). Although changes in joint stiffness were not noted for the hip and ankle in this sample, knee joint stiffness was shown to be different between symptomatic vs. ASYM limbs in individuals with unilateral knee OA (132). This difference suggests the importance of studying a unilateral knee OA sample under different walking conditions.

Although most literature reflects a controlled walking environment, a disconnect is apparent between reported findings in a controlled environment when an individual moves to more unpredictable walking environment that is more reflective of real-world scenarios. To attempt to reflect an unpredictable environment and test the stability of individuals with knee OA, gait perturbations have been used.

2.5 Knee OA Perturbation Research

Many dynamic walking studies are conducted under controlled environments whereby an individual walks in a straight line or on a treadmill, but this is not directly applicable to everyday life where someone is forced to walk on uneven ground and around barriers. Perturbation studies are becoming more common in the literature as a tool to test an individual's gait stability by challenging their walking with unexpected surface translations. By unexpectedly moving the walking surface during single leg support, an individual must compensate for this movement to maintain stability and the mechanism by which the lower limb functions can be studied (49,81–87).

Perturbation studies in the literature undergo a large range of methodologies to apply the perturbation to an individual while walking. A few ways in which a perturbation is applied is through the use of a moveable platform imbedded into a walkway (83,84), manually moving the leg with a strap wrapped around the ankle (142), and through the use of a dual-belt instrumented treadmill (81,85–87). While the range of methodologies has been seen to produce similar results, limitations have been noted when using the moveable platform and manually perturbing the leg. In both studies where a moveable platform was used, Kumar et al. (83) and Schmitt et al. (84) both noted that while the participant was not directly told when a perturbation would occur, they were aware that it would occur when they stepped onto the platform and this could contribute to a preparatory response prior to initial contact. The use of a dual-belt instrumented treadmill does not have similar limitations as the entire walking surface is perturbed. This would ideally eliminate a preparatory response and has been shown to be a reliable gait analysis tool (88).

When laterally perturbing a moveable plate, Kumar et al. did not distinguish any significant differences between individuals with knee OA and ASYM individuals in their response to the perturbations (83). Both groups demonstrated decreased sagittal plane knee motion during the loading response and mid-stance phase of the gait cycle with an increase in muscle activity (83). With similar methodology, Schmitt et al. compared individuals with knee OA who were identified as being stable or unstable (84). No differences in knee motions were identified between the two groups, but the unstable individuals did self report greater knee instability after the perturbations (84). Different muscle activation strategies of higher medial quadriceps-hamstring co-contraction were also noted by the unstable individuals which could indicate a preparatory response (84).

Although these results were thought to be limited using a moveable plate and the development of a preparatory response, similar results have been found when using a dual-belt instrumented treadmill. In preliminary studies using a perturbation protocol comprised of 1 and 3 cm medial and lateral frontal plane perturbations at random with a dual-belt instrumented treadmill, Rutherford et al. found that individuals with knee OA did not biomechanically alter their gait in response to the perturbations (81,87). Alternatively, when performing 2 to 4 cm perturbations at varying speed intensities (ranging from 0.7 to 1.6 m/s), Schrijvers et al. found that individuals with knee OA self-reporting knee joint instability responded to gait perturbations with greater knee flexion angles compared to ASYM individuals during terminal stance, pre-swing of the perturbed stride and the stride after perturbation (86). These identified changes could indicate the importance of a controlled walking speed to monitor perturbation responses. All individuals with knee OA did demonstrate elevated and prolonged muscle activation patterns in direct response to perturbation greater than 2 cm (81,86,87) and is noted with increasing severity of knee OA (49) suggesting a stabilization pattern is used in response to a perturbation (81). Following a series of perturbations occurring in a 30 minute time period, individuals with knee OA demonstrated significantly reduced muscle activation with minimal biomechanical changes once the 30 minute protocol was completed, which indicates that knee joint demand was not increased following the perturbation protocol (85). This gives promise to perturbed walking being a useful rehabilitation tool for individuals with knee OA. Comparing individuals with knee OA to ASYM individuals did not result in any significant group differences indicating that both groups are responding to the perturbation in a similar manner (81,83,85,86).

The support moment or leg stiffness measurements have not been researched as it relates to walking while undergoing surface perturbations in individuals with knee OA and how surface perturbations may affect the lower limb. Investigation into these measurements could potentially identify specific group differences in response to a perturbation as well as provide information on how the whole lower limb is adapting to maintain stability when challenged in individuals with knee OA.

Chapter 3 – General Methodology

The methodology was developed to investigate objectives 1 and 2 outlined in Chapter 1. Recruitment, instrument procedures, analysis procedures and statistical analysis were selected to effectively test these objectives and approved by Nova Scotia Health Authority Research Ethics Board. Data collection and recruitment began in 2015 and have proceeded to present. The author participated in participant recruitment, laboratory set-up, participant set-up, data collection procedures, processing, and data analysis for this thesis. A general methodology is outlined below for the cross-sectional studies and analyses of this thesis.

3.1 Subject Recruitment

3.1.1 ASYM Control Group

The ASYM control group was recruited as a sample of convenience from the community using social media, poster advertisements and email. Interested individuals were contacted by Joint Action Research (JAR) Laboratory researchers and letters were sent to the participants outlining study details. Once interest was confirmed, individuals were contacted via telephone and a standard script was used to determine eligibility. To be eligible, an ASYM participant must have no evidence of OA, be greater than or equal to 50 years of age, no evidence of cardiovascular, neurological, or other musculoskeletal disease or lower limb surgery within the last year.

If the individual was deemed eligible, the participant was scheduled for a 3-hour visit to the JAR Laboratory at Dalhousie University, provided the detailed consent forms, and contact information should they have any questions or concerns prior to their visit.

3.1.2 Participants with Moderate Knee OA

Individuals with MOA were recruited by local orthopaedic surgeons Drs. William Stanish at the Orthopaedic and Sport Medicine Clinic of Nova Scotia and Nathan Urquhart from his orthopaedic practice. Individuals with MOA affecting the medial compartment were diagnosed using the American College of Rheumatology guidelines (143). Physicians connected with eligible participants with a standardized letter of intent explaining why they are being recruited. Participants were asked for permission to transfer their contact information to researchers. Participants were contacted as above, and a standardized script was used for screening. Study eligibility included the same inclusion criteria as the ASYM control group with the addition of being diagnosed with unilateral symptomatic knee pain with radiographic evidence of knee OA, but not be a candidate for total knee replacement. In addition, a participant must be able to walk independently without the use of an ambulatory aid, able to jog 5 meters, able to walk more than a city block, able to climb stairs in a reciprocal fashion and can walk on a treadmill for 30 minutes continuously (31). Once eligibility was determined, the participant was scheduled as above.

3.1.3 Sample Size

In biomechanical studies, specifically involving methodologies using surface perturbations, studies have used varying group sizes ranging from 15-40 individuals

(81,83,85–87,142,144). It is recommended that when estimating the power of a study, a β of 0.2 probability of failing to detect a genuine effect should be used (145). A power of 80 % (Power = 1 – β) was used to calculate the sample size to reject the null hypothesis while reducing the probability of type II error. Zeni et al. have detected a significant difference in peak support moment between self-selected and fast walking speeds in individuals with knee OA of 0.24 Nm/kg (standard deviation = 0.35 Nm/kg) (33). Using the procedure to estimate sample size based on power outlined by Jones et al. (146), a sample size of 19 subjects in each group is required to accurately identify statistical differences when using dependent t-tests. Sample size was also calculated using the G*Power 3 software (latest ver. 3.1.9.7; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) (147,148). Setting the power to 0.8 and assigning a corrected Bonferroni alpha for multiple measurements, a sample size of 35 individuals was determined for each group. An overall sample size of 35 individuals was selected for each group.

3.2 Participant Preparation

Upon arrival, all participants were introduced to the JAR Laboratory going over the procedures, instrumentation, and details of their visit. Consent documents were reviewed, and participants had the opportunity to ask questions prior to obtaining informed consent. Participants completed two questionnaires: the Knee Outcome Survey Activities of Daily Living Scale (KOS-ADLS) and the Knee injury and Osteoarthritis Outcome Score (KOOS). The KOS-ADLS is used to determine functional limitations during daily activities and the KOOS is used to measure a patient's perspectives about their knee in five categories – pain, symptoms, activities of daily living, sport and recreation, and quality of life (149). Following the completion of all forms, participants were asked to change into tight fitting shorts, a t-shirt, and asked to remove footwear. Standard anthropometrics recorded included waist, hip, thigh, and shank circumferences as well as height and weight. Anthropometrics were measured using a measuring tape and a physician beam scale with height rod.

A self-selected walking speed was determined using a GAITRite^{TM} pressure sensitive walkway (CIR Systems Inc., USA). The GAITRite^{TM} has demonstrated validity and high reliability in measuring gait speed (ICC = 0.91-0.99) in younger (88) and older adults (150,151). Participants were instructed to walk at a normal pace over the walkway until five walking trials were recorded. Five walking trials were averaged to calculate the participant's self-selected walking speed used for the perturbation protocol. Participants wore an upper body harness to ensure safety on the treadmill, but not to restrict lower body movement.

Finally, passive retro-reflective surface markers were affixed to participants to monitor the position and orientation of body segments using a standardized procedure (52,81,87) (Figure 3.1). All markers were placed bilaterally. Rigid bodies containing four markers were placed on the head, thorax, pelvis, thigh, and shank. Rigid bodies containing three markers were placed on the forefoot. Individual markers were placed over anatomical boney landmarks of the spinous process of the 7th cervical vertebra, the lateral aspect of the shoulders below the acromion, lateral epicondyle of the elbow, styloid process of the ulna, greater trochanter, lateral and medial epicondyles of the femur and tibia, lateral and medial malleoli, the posterior heel and atop the head of the 1st, 2nd, and 5th metatarsal. A three-marker cluster was also affixed to the right side of the treadmill to track motion during surface translation. Virtual markers were created during calibration for the sternum and left and right anterior superior iliac spine (ASIS).

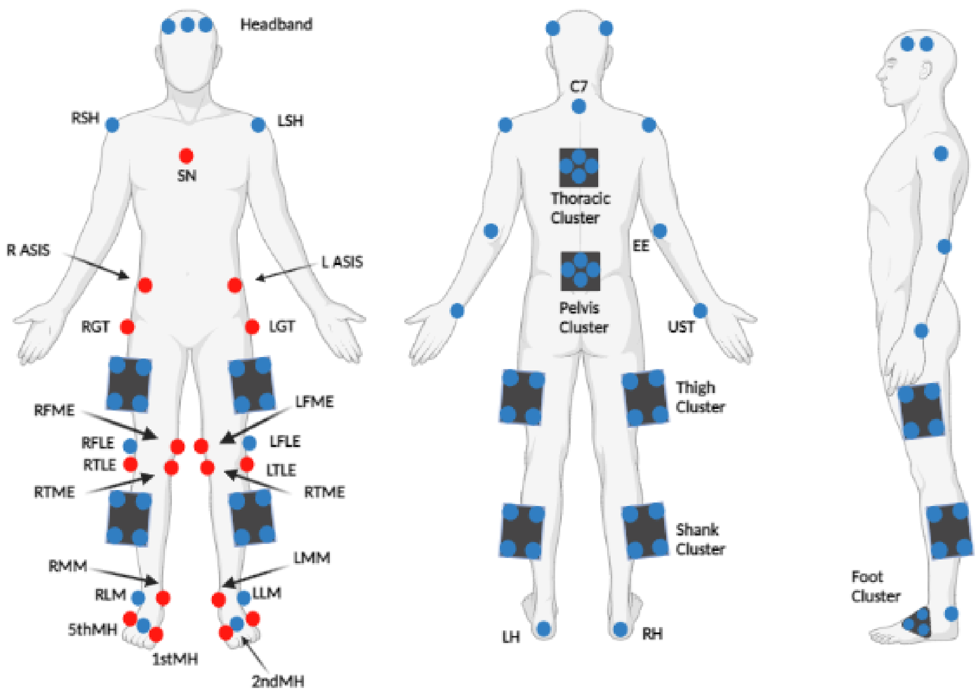

Figure 3.1: Skin surface marker set utilized for this study. Clusters are indicated by grey background with 4 blue balls for the thoracic, pelvis, thigh, and shack, and 3 blue balls for the foot cluster. Virtual point markers are represented by red balls. Individual markers in blue are placed on bony landmarks. Created with BioRender.com.

3.3 Perturbation Protocol

A R-Mill, dual-belt instrumented treadmill was used to conduct the perturbation protocol. Motion of the passive, retro-reflective markers was measured using eight Qualisys® OQUS 500 (Gothenburg, Sweden) motion analysis cameras and sampled at 100 Herts (Hz). Bilateral force plates embedded in the treadmill measured three-dimensional GRFs, sampled at 2000 Hz. Raw surface EMG will be pre-amplified (500 x), and additionally amplified using two AMT-8™ Bortec Systems (Bortec Inc., Canada; bandpass filter 10 – 1000 Hz, Common Mode Rejection Ratio (CMRR): 115 decibels (dB) at 60 Hz, input impedance = ~ 10 GΩ), sampled at 2000 Hz. All signals underwent an analog-to-digital (A/D) conversion (16bit, +/- 5V), and synchronized using Qualisys® Track Manager V2.10 software.

3.3.1 Calibration

A standing calibration was collected with all markers visible. Participants stood on the treadmill facing forward with feed spread to shoulder width apart, and arms on the hand rails. After the calibration trial, the greater trochanters, medial femoral epicondyle, medial and lateral tibial epicondyles, medial malleoli, and 1st and 5th metatarsal markers were removed. Virtual point trials were performed using a pre-calibrated wand to identify the sternal notch and left and right anterior superior iliac spine.

3.3.2 Warm-Up

Prior to the perturbation protocol, participants were harnessed to the ceiling using a rope and upper body harness and made aware of the treadmill safety features. Participants were instructed to walk naturally while remaining in the center of the treadmill with one foot on either force plate, and to keep their head facing forward. Participants proceeded to walk for six minutes at their self-selected walking speed determined by the GAITRite™ as a recommended warm-up (88,152). After their six-minute warm-up, participants were informed the perturbation protocol will commence, but to continue walking normally for approximately 30 minutes.

3.3.3 Perturbation Protocol

The perturbation protocol was comprised of three sets of eight unexpected 1 and 3 cm medial and lateral surface translations (Table 3.1) of the treadmill that occurred at midstance of the leg being tested.

Table 3.1: Perturbation protocol: One set of eight unexpected perturbations. The set is repeated 3 times for a successful protocol.

Perturbation	Leg	Direction	Magnitude (cm)
1	Left	Lateral	1
2	Right	Medial	3
3	Right	Lateral	1
4	Left	Medial	3
5	Right	Lateral	3
6	Left	Lateral	3
7	Left	Medial	1
8	Right	Medial	1

Participants were unaware of the occurrence, direction, or magnitude of the perturbation. The translation was triggered by toe-off of the contralateral leg when less than 50 Newtons (N) of force was detected. The rate of translation was set at 0.1 m/s. After the perturbation occurred, participants walked at least 40 unperturbed strides before another perturbation occurred. During the recorded trial, at least three strides pre- and post-perturbation were monitored. If a cross-over of the contralateral limb onto the opposite force plate, or the participant became unstable and required the handlebars to regain stability during the perturbation occurred, the trial was marked as unsuccessful, and the protocol continued. A total of 24 perturbation trials were recorded if the perturbation protocol was fully completed successfully. Participants then underwent a brief cool-down period once the perturbation protocol was complete.

3.4 Data Processing

3.4.1 Kinematics

Motions were collected using eight Qualisys® motion analysis sensors which monitored the passive retro-reflective marker movement as outlined in section 3.2. To align the camera coordinate system with the force plate coordinate system, all kinematic data were transformed to the treadmill coordinate system using equation 3 where P_{Local} is the point in the local coordinate system, $T_{Treadmill}$ is the transformation matrix of the treadmill coordinate system and P_{Global} is the point in the global coordinate system.

$$P_{Local} = [T_{Treadmill}]^{-1} x \, P_{Global} \tag{3}$$

Kinematic data were low pass filtered (Butterworth 4th order, 6 Hz – recursive) and processed using pre-programmed software (JAR4) which was coded using MatLab 2021b (The Mathworks Inc., Massachusetts, USA). Using this software, the program identified the coordinate systems for the pelvis, thigh, shank, and foot from the retro-reflective skin markers, rigid clusters, and virtual points. Joint angles were calculated using Cardan rotations (153) with order Flexion/Extension, Abduction/Adduction, Internal Rotation/External Rotation. The flexion/extension axis of the hip and knee were oriented in a medio-lateral direction defined by a vector connecting the ASIS and medial and lateral femoral epicondyles. The thigh medio-lateral axis is fixed, and the anterior-posterior and distal-proximal axis were determined by a cross product of the original axes from the greater trochanter to the lateral epicondyle of the femur to define an orthogonal coordinate system. For the shank, the distal-proximal axis is fixed, and the anterior-posterior and medial-later axis were determined by a cross product of the original axes from the lateral to medial malleolus of the shank. The pelvis was determined from the cross between all other axes while the ASIS remains fixed. The hip joint center was estimated using regression equations based on normative data (154). The best predictors for the hip joint center include the pelvic depth for the antero-posterior direction, pelvic width, and leg length for the supero-inferior direction; and the pelvic width for the medio-lateral direction (154). Positive motion was described as flexion, adduction, and internal rotation about the knee joint whereby the distal segment moves about a fixed proximal segment (153). Initial contact and toe-off events were determined using a 30 N vertical GRF threshold whereby a GRF above 30 N indicates initial contact and a GRF before 30 N indicates toe-off (152). Finally, angle waveforms were time normalized to 100 % of the gait cycle.

3.4.2 Kinetics

The instrumented treadmill is comprised of two force plates – one for the left and right feet. Each force place contains 6 sensors that provide three-dimensional GRFs and moments. GRFs and moments were low pass filtered (recursive Butterworth 4th order, 30 Hz) and processed using the preprogrammed JAR4 software written in MatLab 2021b (Mathworks Inc., Massachusetts, USA). As mentioned above, GRFs, kinematics, subject anthropometrics, and inertial properties were used to calculate joint moments using inverse dynamics (117,118).

To derive moments and forces, segments of the thigh, shank and foot were analysed separately and the summation of the external forces and moments acting on each segments' centre of gravity were used to calculate the rate of change of linear and angular momentum (117). Using Newton's Laws of Motion, three-dimensional joint forces and moments were calculated and expressed as specific joint moments on a coordinate system (117). Joint moments were expressed in the same three-dimensional orientation as the kinematic coordinate system, but, a floating axis is created to project the moments into the joint coordinate system (153). Moments were then low-pass filtered (recursive Butterworth 4^{th} order, 10 Hz, normalized to body mass (Nm/kg)), and time normalized to 100 % of the stance phase.

3.5 Data Analysis

The symptomatic leg was chosen for the individuals with knee OA and a random leg was chosen for analysis from the ASYM individuals. Three strides pre-perturbation were averaged for each of the 3cm medial perturbations recorded during the testing to represent a baseline gait for both groups. Since everyone attempted three 3 cm medial perturbations to their symptomatic (or random) leg, there was a potential to average nine pre-perturbation strides if each trial was successful. Individuals who only completed one 3 cm medical perturbation or did not have any successful 3 cm medial perturbations, were not included in the analyses. The first stride post perturbation was also extracted for a maximum of 3 strides if each trial was successful. Ensemble averages were calculated from the three strides pre-perturbation (T0) and the stride immediately after perturbation

(T1) for at least two of the three 3 cm medial perturbation bouts for each participant. In addition, baseline measurements were extracted for Objective 2 to investigate a standard of reference for leg stiffness. Baseline measurements was recorded after the 6-minute warm-up and was comprised of approximately 15 strides averaged to create a baseline ensemble averaged. For this investigation only information pertaining to the sagittal plane was extracted.

3.5.1 Support Moment Analysis

Sagittal plane internal moments of the hip, knee and ankle were extracted for T0 and T1 when a 3cm medial perturbation occurred on the affected limb. The support moment was calculated by equation 1 (*2.3.2 Support Moment*). The peak support moment during the first half of stance (0—50% of the stance phase) was extracted. The position during stance phase at which the peak support moment was identified was used to calculate hip, knee, and ankle joint moment contributions as a percentage of the peak support moment (155) at T0 and T1. The peak support moment, position, and percent joint moment contributions were compared at T0 and T1 for individuals with knee OA and ASYM individuals to determine the response to the perturbation.

3.5.2 Leg Stiffness Analysis

Leg stiffness was calculated using custom MatLab R2021a script developed for the purpose of this thesis' data analysis. Leg stiffness was calculated as mentioned in section 2.5.2 using equation 2 which results in the comparison of a single value. Leg stiffness was calculated for each stride in all trials. Sample plots of the ground reaction force and leg length vs. percent stance phase are shown in Appendix B. Ensemble averages of leg stiffness were calculated at baseline, T0 and T1. A comparison between the baseline and T0 leg stiffness measurements were used to determine a standard of reference value for leg stiffness. T0 and T1 leg stiffness measurements were compared both within and between groups to determine the response to the perturbation and identified differences in leg stiffness between individuals with knee OA and ASYM individuals.

3.6 Statistical Analysis

All statistical analysis were performed using IBM® SPSS® Statistics 27 (SPSS). Normality and equal variance were determined by the central limit theorem and Levene's test, respectively. Independent t-tests were used to test for significant group differences in subject characteristics, including age, height, sex, body mass index (BMI), walking velocity, and KOOS measurements. Results of the independent t-tests were used to provide insight on any differences between the two groups, with optimal results suggesting there are no significant difference in subject characteristics that could influence the biomechanical analysis. Individuals with knee OA and ASYM individuals were attempted to be matched by age, sex distribution, and walking velocity.

The support moment analysis focused on differences from T0 to T1 to gauge the response of the lower limb in individuals with knee OA and ASYM individuals. Dependent t-tests were used to test for significant within group differences between T0 and T1 for peak support moment, hip, knee, and ankle percent support moment contributions, and percent stance position of the peak support moment for both groups. P values were set to a significance level of $\alpha = 0.05$. Effect sizes (d) were reported based on Cohens d.

The leg stiffness analysis focused on determining a standard of reference value of leg stiffness when using a dual-belt instrumented treadmill as well as determining both within and between group affects of leg stiffness in response to the perturbation for individuals with knee OA and ASYM individuals. A mixed model analysis of variance (ANOVA) was used to determine the response to the perturbation by analysing between group differences as well as within group differences of repeated measures between baseline, T0, and T1. Mauchly's test of sphericity was used to test for the homogeneity of the covariances. Effect sizes (η^2) were reported based on Partial Eta Squared. Post-hoc testing was conducted using dependent t-tests to measure within group differences between baseline and T0 and T0 and T1 for both individuals with knee OA and ASYM. A Bonferroni alpha correction was used for post-hoc testing accounting for 4 tests. P values were set to a Bonferroni alpha equal to 0.013. Effect sizes (d) were reported based on Cohens d.

Chapter 4 - The Biomechanical Response to Unexpected Walking Surface Translations During Gait in Individuals with Knee Osteoarthritis: Support Moment Analysis.

4.1 Introduction

Knee OA is a debilitating disease with individuals effected commonly reporting subjective outcome measures of associated pain, instability, and activity limitations such as walking (96,97). In unison, individuals with knee OA have demonstrated significant differences in kinematics, kinetics, and muscle activation patterns during gait when compared to ASYM individuals. Specifically, in the sagittal plane, individuals with knee OA are consistently reported to walk with a reduced knee ROM (40,52,53) and a decrease in the external knee flexion-extension dynamic moment (32,43,48). Through these notable changes in sagittal plane biomechanics, individuals with knee OA are thought to have a reduced ability to unload the joint during midstance and are thought to walk with a "stiff knee" gait in an attempt to gain stability during stance (40,48,55).

While studies of individuals with knee OA commonly report effects on the knee joint, an integrated synergy of the entire lower limb is required to maintain walking (156). The support moment, which sums the net internal extension sagittal plane moments at the major lower limb joints (equation 1, section *2.3.2 Support Moment*) – hip, knee, and ankle – has been used to represent the total limb pattern to push away from the ground (156) and can be thought of as the net moment that prevents collapse during weight bearing activities (66–68). Current literature has suggested individuals with knee OA walk with a decreased support moment (69–71) which could be related to a slower gait speed identified in individuals with knee OA (70) as well as indicate a possible strategy to minimize the impact of the GRFs on the lower extremity (71). Additionally, studies have quantified the contributions of the hip, knee, and ankle as a percentage of the peak support moment to understand potential control strategies used to coordinate movement (155). Together, a support moment analysis provides the opportunity to understand the integrated synergies required to support walking.

Knee biomechanical outcomes during gait conclude that alterations exist while walking to maintain function as people navigate their environment. Walking perturbation studies have been used to understand what alterations to gait may occur in the context of maintaining function when challenges are imposed during the gait cycle (81,82,86,87). Most common perturbations consist of medial and lateral walking surface translations applied during the stance phase of gait. Perturbation study outcomes support that individuals with mild to moderate knee OA and ASYM individuals immediately respond to a frontal plane walking surface translation with increased knee joint muscle activation with minimal changes to biomechanical outcomes. This suggests a preservation of knee joint function to maintain forward walking trajectories but no significant biomechanical alteration were noted (81,86,87). However, it is presumed that compensations can occur in the lower extremity that may not be directly manifested at the knee joint. Whether a change of the main support mechanisms of the lower limb in response to walking perturbations occurs has yet to be established. Additionally, whether individuals with knee OA and ASYM individuals reorganize this response differently between the hip, knee, and ankle joint is unknown.

The main objective of this study was to determine whether the peak support moment and percent contributions from the hip, knee, and ankle were altered with an unexpected 3 cm medial walking surface translation during stance for ASYM individuals and individuals with knee OA. The hypotheses were that both groups would increase their peak support moment in response to the unexpected walking surface translation, but individuals with knee OA will respond to the surface translation with an increase in the hip percent contributions that acts to decrease the knee percent contributions in response to the perturbation. ASYM individuals will show no significant changes in percent joint contributions in response to the perturbation.

4.2 Methodology

4.2.1 Participant Selection

As presented in Chapter 3, thirty-five individuals with unilateral symptomatic knee OA were recruited through consultation with an orthopaedic surgeon. Individuals with knee OA were diagnosed using the American College of Rheumatology guidelines (143) and self-reported a functional capacity in line with a moderate knee OA diagnosis (31). Participants were excluded if they were considered a candidate for total knee replacement. Thirty-five older adults (ASYM individuals) who reported no signs or symptoms of musculoskeletal injury or disease were recruited as a sample of convenience from the local community. All individuals were above 50 years of age, did not have a fracture or current lower extremity injury, no neurological or cardiovascular disorder that would impair walking ability and able to walk independently for at least 30 minutes. The protocol was approved by local institutional ethics committee (Nova Scotia Health, Halifax, Canada).

4.2.2 Perturbation Protocol

Participants were asked to change into tight fitting shorts, t-shirt, and asked to remove footwear. Consent was obtained and participants completed the KOS-ADLS and KOOS (149). Five randomly recorded walking trials were performed using the GAITRite^{TM} (CIR Systems Inc., USA) to determine the average self-selected walking speed (88).

Passive retro-reflective surface markers were affixed to participants (Figure 3.1) to monitor the position and orientation of body segments using a standardized procedure (52,81,87). Rigid bodies containing four markers were placed on the head, thorax, pelvis, thigh, and shank. Rigid bodies containing three markers were placed on the feet. Individual markers were placed on remaining, predefined, anatomical boney landmarks of the arms and legs. Motion of the passive, retro-reflective markers will be measured using eight Qualisys® OQUS 500 (Gothenburg, Sweden) motion analysis cameras and sampled at 100 Herts (Hz).

Participants walked for 6 minutes at their self-selected walking speed determined by the GAITRite^{TM} as a recommended warm-up (88,152). GRFs were sampled from the treadmill at 2000 Hz during walking and synchronized with motion capture marker trajectories using Qualisys® Track Manager V2.10 software. Participants then underwent approximately 30 minutes of perturbed walking whereby three sets of eight unexpected 1 and 3 cm medial and lateral surface translations of the treadmill occurred at midstance of either the right or left leg (81), as described in the methodology section of Chapter 3. The translation was triggered by toe-off of the contralateral leg when less than 50 Newtons (N) of force was detected with a rate of translation of 0.1 m/s (81). Participants were instructed to remain walking without the use of the handrails while keeping their feet on either belt during and in response to the perturbation. Trials where handrails were used, or footfalls crossed onto the opposite plate were excluded. During the recorded trial, at least three strides pre-perturbation and one stride post-perturbation were recorded.

4.2.3 Data Processing

Custom programs written in MatLab 2021b (The Mathworks Inc., Massachusetts, USA) were used to process all data (81,82,88). Moments were calculated using inverse dynamics, low pass filtered (recursive Butterworth 4^{th} order, 10 Hz, normalized to body mass (Nm/kg)), and time normalized to 100 % of stance phase (beginning at initial contact and ending at toe off). The support moment was calculated through stance phase for T0 and T1 for all successful 3 cm medial perturbation bouts using equation 1 (Section *2.3.2 Support Moment*).

4.3 Statistical Analysis

Thirty-five individuals with knee OA and 35 ASYM individuals were identified to have successfully completed at least 2 or more successful 3 cm medical surface perturbations. Of the 70 identified participants, one participant was excluded from the statistical analysis because of inaccurate knee moment waveforms. In total, 34 individuals with knee OA and 35 ASYM individuals were used for statistical analysis.

The symptomatic leg of the individuals with OA and a random leg of the ASYM individuals were selected for analyses. The peak support moment between 0 – 50 percent of stance phase was identified for T0 and T1. The position during stance phase at which the peak support moment was identified was used to calculate hip, knee, and ankle joint moment contributions to the peak support moment (155). The hip, knee, and ankle moment contributions were expressed as a percentage of the peak support moment.

Normality and equal variance were determined by the central limit theorem and Levene's test respectively. Independent t-tests were used to test for significant between group differences in subject characteristics, including age, height, sex, BMI, walking velocity, and KOOS measurements. In addition, dependent t-tests were used to test for significant differences between T0 and T1 for peak support moment, hip, knee, and ankle percent support moment contributions, and percent stance position of the peak support moment for both groups. P values were set to a significance level of $\alpha = 0.05$. Effect sizes (d) were reported based on Cohens d. All statistical procedures were completed using SPSS.

4.4 Results

Individual participant hip, knee, and ankle sagittal plane moment waveforms are presented in Appendix A. Participant characteristics, including participant demographics, walking speed, and KOOS questionnaire outcomes are shown in

Table 4.1.

Table 4.1: Mean (standard deviation) participant characteristics.

	ASYM	Knee OA
Variable		
n	35	34
Age (years)	60.7 (6.6)	61.1 (6.6)
Sex (M:F)	18:17	18:16
Height (m)	1.69 (0.08)	1.69 (0.10)
Mass (kg)	71.8 (13.7)*	86.8 (14.9)*
BMI (kg/m^2)	25.1 (3.7)*	30.2 (4.5)*
Walking Velocity (m/s)	1.16 (0.10)*	1.09 (0.10)*
KOS giving way score	[33]5 - [2]4	[10]5 - [8]4 - [7]3 - [8]2 - [1]1
KOOS		
Symptoms (n/100)	98 (4)*	59 (14)*
Pain (n/100)	99 (3)*	65 (16)*
Activities of Daily Living (n/100)	100 (1)*	69 (19)*
Quality of Life (n/100)	97 (5)*	47 (18)*

BMI – Body Mass Index.

KOS – Knee Outcome Survey

KOOS – Knee Osteoarthritis Outcome Score.

* Indicates a significant difference between groups $p < 0.5$.

Individuals with knee OA had a greater mass ($p < 0.001$), greater BMI ($p < 0.001$), and walked at a slower self-selected speed ($p = 0.016$). There were no between group differences in age ($p = 0.814$). Analyzed metrics of the peak support moment, percent joint moment contributions (hip, knee, and ankle), and position during stance are summarized in Table 4.2 for T0 and T1.

Table 4.2: Mean (Standard Deviation) peak support moment and relative percent joint moment contributions. Reported dependent t-test significance and Cohen's d.

Variables	Knee OA				ASYM			
	T0	T1	*p*	Cohen's d	T0	T1	*p*	Cohen's d
Support Moment (Nm/kg)	0.73 (0.28)*	0.90 (0.31)*	<.001	-0.863	0.94 (0.44)*	1.10 (0.42)*	<.001	-0.880
Hip Percent Contribution (%)	50.03 (32.35)*	41.54 (23.42)*	0.01	0.470	50.12 (28.15)*	41.65 (25.24)*	0.045	0.351
Knee Percent Contribution (%)	24.54 (34.09)*	14.41 (27.82)*	0.003	0.555	29.59 (36.46)*	15.01 (27.81)*	<.001	0.824
Ankle Percent Contribution (%)	25.43 (21.37)*	44.05 (23.07)*	<.001	-1.330	20.29 (18.84)*	43.35 (25.10)*	<.001	-0.946
Stance Phase Position (% Stance Phase)	24.44 (4.27)*	26.35 (4.70)*	0.001	-0.609	23.63 (2.57)*	26.26 (5.50)*	0.008	-0.476

** Indicates a significant difference within groups p < 0.05.*

4.4.1 Support Moment

Ensemble average waveforms for each group of the support moment during a 3 cm medial perturbation at T0 and T1 is shown in Figure 4.1. A distinct peak in the support moment is identified during early stance for both groups at T1 and T0.

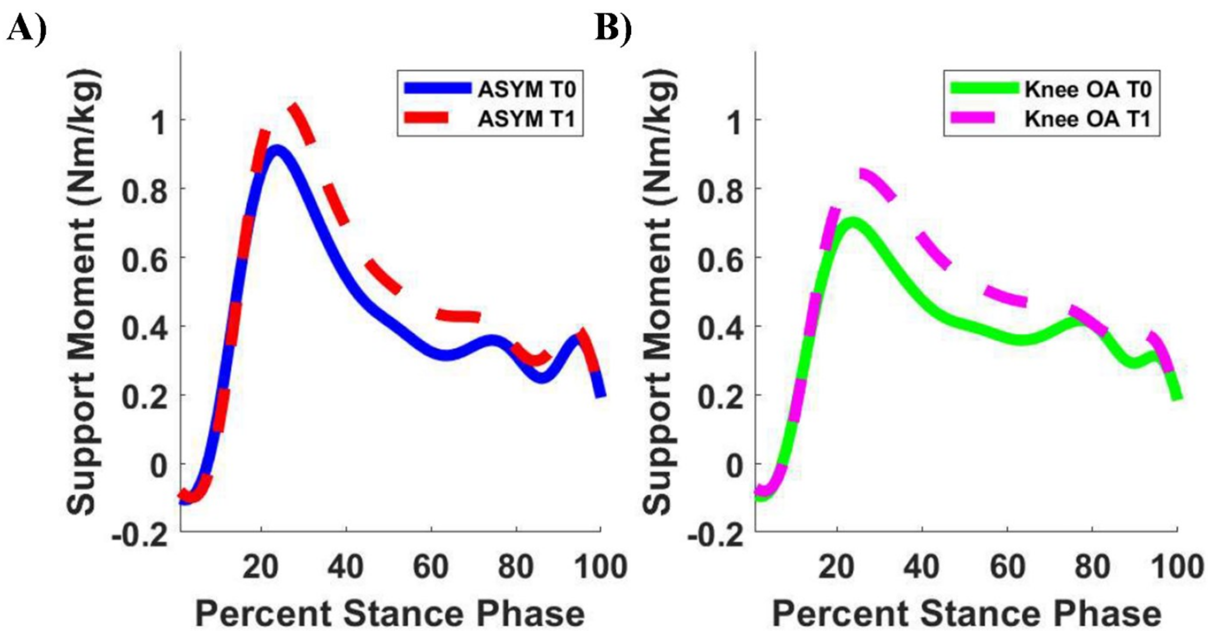

Figure 4.1: Ensemble averaged support moment waveforms for ASYM individuals (A) and individuals with knee OA (B) at T0 and T1 time normalized to stance phase and amplitude normalized to body mass.

The peak support moment was greater at T1 compared to T0 in both groups (individuals with knee OA ($p = <0.001$, $d = -0.863$) and ASYM individuals ($p = <0.001$, $d = -0.88$)). Similarly, the position at which the peak support moment was identified was significantly later during stance phase in both groups ($p < 0.017$), where at T0 the peak occurred at approximately 24% of stance phase and T1 at approximately 26% of the stance phase for both groups. For the entire data set, the peak support moment was reported to occur after

15 % of stance phase (i.e. during mid stance), indicating it did not occur when the perturbation was occurring (i.e., while the treadmill was in motion) (81).

4.4.2 Hip, Knee, and Ankle Percent Joint Moment Contributions

Figure 4.2 depicts the joint moment contributions from the hip, knee, and ankle as a percentage of the peak support moment at T0 and T1.

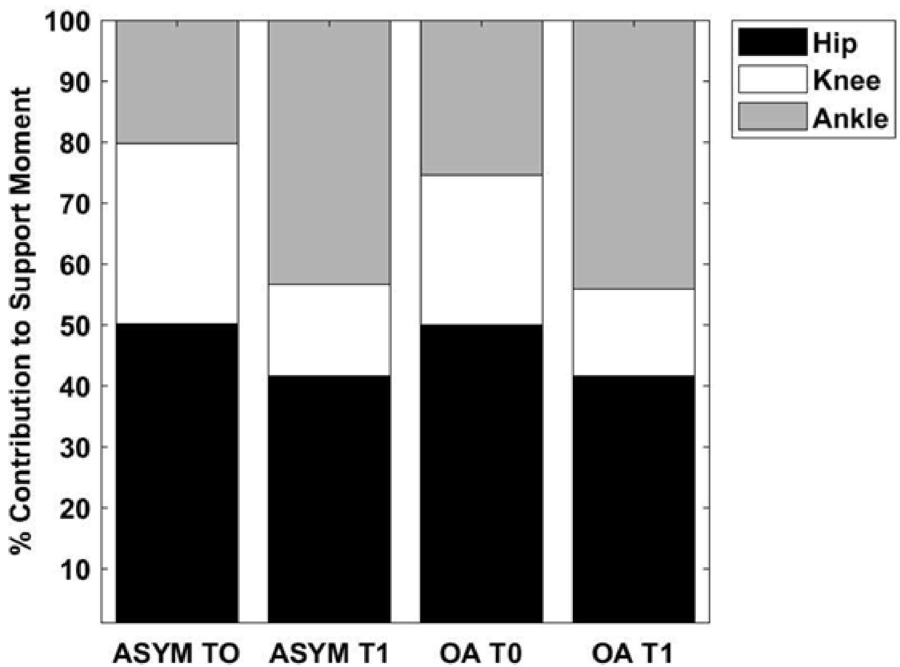

Figure 4.2: Percent hip, knee, and ankle joint moment contributions of the peak support moment at T0 and T1 for ASYM individuals and individuals with knee OA.

Percent contributions to peak support moment increased for the ankle ($p = <0.001$, $d = -0.946$) and decreased for the knee ($p = <0.001$, $d = 0.824$) and hip ($p = 0.045$, $d = 0.351$) at T1 compared to T0 in ASYM. Individuals with knee OA followed the same pattern whereby percent contributions to peak support moment increased for the ankle ($p = <0.001$, $d = -1.326$) and decreased for the knee ($p = 0.003$, $d = 0.555$) and hip

($p = 0.01$, $d = 0.47$) at T1 compared to T0.

4.5 Discussion

This study aimed to determine whether the peak support moment and percent contributions from the hip, knee, and ankle were altered in response to an unexpected 3 cm medial walking surface translation during stance for ASYM individuals and individuals with knee OA. The hypotheses were that both groups would increase their peak support moment in response to the unexpected walking surface translation, but individuals with knee OA will respond to the surface translation with percent contributions of the hip, knee, and ankle joints that are different from ASYM individuals, indicating a different control strategy implemented. Study results partially support the proposed hypotheses whereby both groups increased their peak support moment in response to the perturbation, but both groups were found to respond using a similar control strategy. Individuals with knee OA and ASYM individuals both increased their peak support moment in response to the perturbation and the greater support moment was also apparent further into stance phase than pre-perturbation. Both groups did this by reorganizing the contributions of the major lower limb joints where the knee and hip contributions were significantly reduced, and the ankle contribution was significantly increased.

Detailed in Table 4.1, similarities existed between groups for age, sex distribution, and height. Individuals with knee OA additionally replicated characteristic trends associated with knee OA, and commonly reported in the literature, where they demonstrated a significantly higher mass and BMI, a slower walking velocity, and lower KOOS scores compared to ASYM individuals (81,85). While a slower walking velocity was identified, the difference between individuals with knee OA and ASYM individuals was less than the minimal detectable change (0.09 m/s) indicating the difference in walking velocity could likely be due to chance variation (88) and not an influence on study results. Individuals with knee OA also reported more episodes of giving way of the knee joint which affected their daily activity as determined by the KOOS. With similar characteristics identified, the selected knee OA cohort has been confirmed to be characteristic of individuals with mild to moderate knee OA.

To analyse trends in peak support moment and percent hip, knee, and ankle joint moment contributions seen in both the individuals with knee OA and ASYM cohort, dependent t-tests were used to determine differences between T0 and T1 to characterize the control strategy employed to successfully complete the 3 cm medial perturbation. The identified support moment waveform (Figure 4.1) and peak support moment for individuals with knee OA and ASYM individuals resembled values reported by Zeni and Higgins (69). The support moment measurement has been found to be less variable than individual joint moments and more reproducible when comparing across the literature (156,157). The increase in peak support moment in response to the perturbation (Table 4.2) indicates that all individuals were forced to increase the load placed on the effected lower limb to prevent collapse and maintain single limb stability during stance. It also took slightly longer in stance phase for an individual to maintain stability after experiencing the perturbation (Table 4.2). While individuals with knee OA are being forced to increase the load on the lower limb in response to the perturbation, they did not report an increase in pain after 30 minutes of perturbed walking (85). This indicates that an increased load to the lower limb could be implemented through a reorganized control strategy not involving increased loads at the knee joint. Seeley et al., suggests that a reduced peak support moment indicates a reduction in the lower limb's ability to resist gravity and prevent collapse (158). Previous studies have found individuals with knee OA walk with a lower peak support moment compared to an ASYM cohort (69,70,158) and also commonly report knee instability such as buckling and giving way (40,55,58). The greater support moment found in both groups would suggest a strategy to resist gravity, prevent limb collapse, and perhaps, maintain stability was adopted in response to the walking perturbation in the current study.

The support moment can further be separated into percent hip, knee, and ankle joint moment percent contributions of the peak support moment (Figure 4.2) to investigate the control strategies utilized to coordinate movement in response to the perturbation (159). Both individuals with knee OA and ASYM individuals were found to significantly decrease the hip and knee contributions to the peak support moment while increasing the ankle contribution from T0 to T1 (Table 4.2). While the analysis of the joint moment contributions resulted in large standard deviations, medium to large effect sizes were still reported for each comparison. Comparing the measured joint moment contributions at T0 to those reported by Zeni and Higgins (69), our knee OA and ASYM samples reported visibly higher hip contributions, and a visibly lower ankle contribution at the self-selected speed. These outcomes contradict other evidence that individuals who are projected for a total knee replacement walk with a larger hip contribution to compensate for a decrease in knee contribution (160). The outcome differences could potentially be due to the high reported variability in individual joint movement patterns (156,157).

The knee joint contribution decreased in response to the perturbation in both the knee OA and ASYM cohorts (Table 4.2, Figure 4.2). A reduction in knee joint contribution has been attributed to limiting the internal knee extension moment generation during walking to reduce knee joint loading or as an effect of quadricep weakness (69,159,161). This is further supported by previous perturbation studies that have identified less dynamic quadricep activity in response to a 3 cm medial perturbation (81). Although individuals with knee OA reduced the knee joint contributions, this has not been found to correlate with reduced tibiofemoral joint contact forces in individuals with knee OA (69) or individuals with other knee pathologies (161). Finally, at T1, the knee joint was only responsible for approximately 15 % contribution to the support moment in both groups, leading to the conclusion that the knee joint is not as involved in providing sagittal plane support compared to hip and ankle contributions after the medial perturbation (160). Therefore, a decrease in knee contribution could be indicative of a knee stiffening strategy employed in response to the medial perturbation.

Previous studies have identified that the support moment was largely produced by the ankle contributions during single limb support (162,163). Simosen et al., has suggested that under normal walking conditions, a large internal plantar flexion moment about the ankle could result in the generation of a external knee flexion moment to maintain joint angle positions and fluidity in movement (164). Therefore, the increase in ankle contribution in response to the perturbation might not only be acting as a compensatory mechanism in response to the decrease in knee contribution, but in turn could be causing additional decrease in the knee contribution because of the perturbation. This relationship could indicate why similar trends are observed between individuals with knee OA and ASYM individuals when analysing the changes in knee and ankle contributions from T0 to T1. This prediction is further supported by an identified elevated and prolonged gastrocnemius activity in response to the perturbation (81). In addition, in both unperturbed and perturbed walking studies, the centre of mass has been noted to regulate mediolateral foot placement (165). Foot placement has further been suggested to be the dominant mechanics for maintaining stability during gait in the frontal plane (165). In response to the medial perturbation, both groups of individuals could be increasing their ankle contributions to control the centre of mass that is further displaced by the medial perturbation. This control could be achieved by moving the centre of pressure and generating a resultant dominating ankle joint moment (165). Overall, this would suggest that in response to a 3 cm medial perturbation, both groups are placing greater demand on the ankle.

Finally, both groups significantly decreased the hip contribution between T0 and T1 (Table 4.2, Figure 4.2). One reported lower limb strategy used to compensate for knee pathologies has been coined the “hip strategy” where a reduced knee support moment corresponds with an increase in the hip support moment contribution (160,161). This strategy was not shown to be implemented in response to the perturbation. Instead, it could be possible that during a medial perturbation, the response of the lower limb is transmitted proximally from the ankle and is based on the response of the ankle. As mentioned, the ankle could be creating a decrease in the knee joint contribution in order to maintain a fluid walking pattern (preventing a stiff and extended knee) (164). The knee and hip contributions have also been shown to demonstrate variable trade off between moment patterns depending on individuality in walking patterns (156,157). Therefore, it could be proposed that individuals are significantly decreasing their knee contributions in response to an increase in ankle contribution paired with an attempt to unload the knee joint and the hip follows suit to maintain motion. In addition, the decrease in hip contribution seen in ASYM individuals potentially demonstrated a higher variability because the knee and hip were able to more fluidly trade off contributions for any given response (156,157).

Results in this study must be interpreted considering certain limitations. Individuals were filtered on the premise that they were able to complete at least 2/3 successful 3 cm medial surface perturbations. Every participant was able to complete the perturbation testing; however, crossing onto the other plate or grabbing the handrails in response to the perturbation was deemed an unsuccessful trial. Theoretically, the more failed attempts at completing the perturbation could indicate that the individual is more unstable in response to a 3 cm medial perturbation. By removing all individuals who only completed one successful trial or did not successfully complete any trials, we are potentially missing changes in control patterns that could be utilized in a more unstable group. Additionally, by removing trials where a person was unsuccessful could be inadvertently manipulating the data set to show a more similar pattern in movement between individuals with knee OA and ASYM individuals. Previously, it was found that ASYM and knee OA groups had similar numbers of successful responses using the using the current walking perturbation paradigm (81). Finally walking velocity was not controlled for within this sample. An increase in walking velocity has been found to demonstrate changes in the support moment and percent joint moment contributions (69) as well as elicit changes in foot placement during walking (165). Self selected walking velocity and the impact this may have on control strategies used in response to walking perturbations requires further study in older adults and individuals with knee OA.

4.6 Conclusion

In summary, both individuals with knee OA and ASYM individuals responded to the 3 cm medial walking perturbation in a similar way. Both groups significantly increased their support moment in response to the perturbation and walked with a reorganized control strategy at T1 involving a decrease in the hip and knee joint contribution and corresponding increase in ankle joint contribution. Both groups required more support from the lower extremity (hip, knee, and ankle) to maintain walking immediately after experiencing a 3 cm medial perturbation and accomplished this by reorganizing their support moment joint moment contributions. It is proposed that the knee joint is not readily involved in maintaining support in response to the medial perturbation as both groups significantly decreased their knee joint contributions. Alternatively, the ankle was shown to dominate support which suggests a greater demand was put on the ankle in response to the walking perturbation.

Chapter 5 - The Biomechanical Response to Unexpected Walking Surface Translations During Gait in Individuals with Knee Osteoarthritis: Leg Stiffness Analysis.

5.1 Introduction

Knee OA is a debilitating disease with associated effects including pain, instability and limitations during activities such as walking (96,97). Throughout the literature, individuals with knee OA have demonstrated significant changes in kinematics, kinetics and muscle activation during gait when compared to ASYM older adults. A "stiff knee gait" has been coined to describe how individuals with knee OA walk and is representative of a decrease in the sagittal plane moment dynamics (133) and corresponding increase in knee joint stiffness (53,132). The "stiff knee gait" is thought to help stabilize the knee joint through stance to combat a reduced ability to unload the knee joint during stance (48,60,61) and could play a role in increasing stability (134).

While notable differences at the knee joint have been reported in individuals with knee OA, an integrated synergy of the entire lower limb is required to support walking (156). Stiffness is defined as the extent to which an object resists deformation in response to an applied force (131). Leg stiffness can be used to study the effects of knee OA on the whole lower limb opposed to solely the knee joint and can be thought to represent the control of the musculoskeletal system on the lower limb (78). Leg stiffness can thus be thought of as the ability of the lower limb to resist collapse in response to an applied force. Within this definition, leg stiffness can be maintained by an increase in the skeletal component by decreasing the flexion of the lower limb joints, or by increasing the muscular component by increasing muscle activity and resulting joint moments (78). Leg stiffness is measured as the ratio of peak vGRF over the change in leg length during stance phase (72). Leg stiffness was calculated as mentioned in section 2.5.2 using equation 2 (72).

Current literature has not reported a standard of reference for leg stiffness (139,140), but within study comparisons should produce comparable values. Conflicting reports of leg stiffness measurements in individuals with knee OA have been made whereby some findings have supported that individuals with knee OA have a greater leg stiffness compared to ASYM individuals (78) and others have reported a lower leg stiffness (166). Differences in results could be attributed to the various components that influence leg stiffness such as walking speed (78), peak vGRF (77), muscular control (167) and specific computations. Further investigation into leg stiffness measurements provides an opportunity to better understand the effects of knee OA on the lower limb.

Walking perturbation studies have been used to understand what alterations to gait may occur to maintain walking when challenges are imposed during the gait cycle (81,82,86,87). Perturbation study outcomes support that both individuals with mild to moderate knee OA and ASYM individuals immediately respond to a frontal plane walking translation with increased knee joint muscle activation (81,86,87) but demonstrate similar knee biomechanics in response to the perturbation (81). This would indicate that individuals with knee OA were able to functionally perform similarly to ASYM individuals when presented with alterations to gait. Whether a change in lower limb leg stiffness in response to walking perturbations occurs has yet to be established. Additionally, whether individuals with knee OA and ASYM individuals walk and respond with similar leg stiffness measures remains undetermined.

The main objective of this exploratory study was to determine reference values for leg stiffness in individuals with knee OA and older adults and whether leg stiffness was altered immediately after the application of an unexpected 3 cm medial walking surface translation during stance for individuals with knee OA compared to ASYM individuals. The hypotheses were that both individuals with knee OA and ASYM individuals would have similar baseline and T0 leg stiffness values. Additionally, that both groups would increase their leg stiffness in response to unexpected walking surface translations, and individuals with knee OA would have an overall lower leg stiffness during normal walking when compared to ASYM individuals.

5.2 Methodology

5.2.1 Participant Selection

As outlined in Chapter 3, thirty-five individuals with unilateral symptomatic knee OA were recruited through consultation with an orthopaedic surgeon. Individuals with knee OA were diagnosed using the American College of Rheumatology guidelines (143) and self-reported a functional capacity in line with a moderate knee OA diagnosis (31). Participants were excluded if they were considered a candidate for total knee replacement. Thirty-five older adults (ASYM individuals) who reported no signs or symptoms of musculoskeletal injury or disease were recruited as a sample of convenience from the local community. All individuals were above 50 years of age, did not have a fracture or current lower extremity injury, no neurological or cardiovascular disorder that would impair walking ability and able to walk independently for at least 30 minutes. The protocol was approved by local institutional ethics committee (Nova Scotia Health, Halifax, Canada).

5.2.2 Perturbation Protocol

Participants were asked to change into tight fitting shorts, t-shirt, and asked to remove footwear. Consent was obtained and participants completed the KOS-ADLS and KOOS (149). Five randomly recorded walking trials were performed using the GAITRite™ (CIR Systems Inc., USA) to determine the average self-selected walking speed (88).

Passive retro-reflective surface markers were affixed to participants (Figure 3.1) to monitor the position and orientation of body segments using a standardized procedure (52,81,87). Rigid bodies containing four markers were placed on the head, thorax, pelvis, thigh, and shank. Rigid bodies containing three markers were placed on the feet. Individual markers were placed on remaining, predefined, anatomical boney landmarks of the arms and legs, including the spinous process of the 7th cervical vertebra, the lateral aspect of the shoulders below the acromion, lateral epicondyle of the elbow, styloid process of the ulna, greater trochanter, lateral and medial epicondyles of the femur and tibia, lateral and medial malleoli, the posterior heel and atop the head of the 1st, 2nd, and 5th metatarsal. Motion of the passive retro-reflective markers was measured using eight Qualisys® OQUS 500 (Gothenburg, Sweden) motion analysis cameras and sampled at 100 Herts (Hz).

Participants walked for 6 minutes at their self-selected walking speed determined by the GAITRite™ as a recommended warm-up (88,152). At 6 minutes, a recorded trial of 15 to 20 strides was measured to indicate baseline walking properties. Ground reaction forces were sampled from the treadmill at 2000 Hz during walking and synchronized with motion capture marker trajectories using Qualisys® Track Manager V2.10 software.

Following the warmup, participants underwent approximately 24 minutes of walking whereby three sets of eight unexpected 1 and 3 cm medial and lateral surface translations of the treadmill occurred at midstance of either the right or left leg (81), as outlined in detail in Chapter 3. The translation was triggered by toe-off of the contralateral leg when less than 50 N of force was detected with a rate of translation of 0.1 m/s (81). Participants were instructed to remain walking without using the handrails while keeping their feet on either belt in response to the perturbation. Trials where handrails were used, or footfalls crossed onto the opposite plate were excluded.

5.2.3 Data Processing

Custom programs written in MatLab 2021b (Mathworks Inc., Massachusetts, USA) were used to process all data (81,82,88). Leg stiffness was calculated using equation 2 (section *2.4.2 Leg Stiffness*) at baseline, T0 and T1 using custom MatLab R2021a script. The peak vGRF (N) was identified in the early half of stance (Figure B.1) and normalized to body weight (N). An average location of 4 pelvis markers and the posterior calcaneus marker position data was used to create a vector to measure dynamic leg length during gait. Figure B.2 demonstrates a representative leg length pattern over stance phase. L_0 was identified as the initial leg length at the start of stance phase and L_{min} was demonstrated at terminal stance when the calcaneus was slightly raised from the treadmill surface. The change in leg length was thus represented as the change throughout stance phase. Leg stiffness was calculated for each stride in all trials. Ensemble averages of leg stiffness were calculated at baseline, T0, and T1 for all successful 3 cm medial perturbations.

5.3 Statistical Analysis

Thirty-four individuals with knee OA and 35 ASYM individuals were identified to have successfully completed at least 2 or more successful 3 cm medical surface perturbations. The symptomatic leg of the individuals with knee OA and a random leg of the ASYM individuals was selected for statistical analyses. Leg stiffness was calculated, and ensemble averaged at baseline, T0, and T1 for individuals with knee OA and ASYM. All statistical procedures were completed using SPSS.

Normality and equal variance were determined by the central limit theorem and Levene's respectively. Independent t-tests were used to test for significant between group differences in subject characteristics, including age, height, sex, BMI, walking velocity, and KOOS measurements ($\alpha = 0.05$). A mixed model ANOVA was used to determine between group differences as well as within group differences of repeated measures between baseline, T0, and T1. Mauchly's test of sphericity was used to test for the homogeneity of the covariances. Effect sizes (η^2) were reported based on Partial Eta Squared. Post-hoc testing was conducted using dependent t-tests to measure within group differences between baseline and T0 and T0 and T1 for both individuals with knee OA and ASYM. A Bonferroni alpha correction was used for post-hoc testing accounting for 4 tests. P values were set to a Bonferroni alpha equal to 0.013. Effect sizes (d) were reported based on Cohens d.

5.4 Results

Participant characteristics, including participant demographics, walking speed, and KOOS questionnaire outcomes are shown in Table 5.1.

Table 5.1: Mean (standard deviation) participant characteristics.

	ASYM	Knee OA
Variable		
n	35	34
Age (years)	60.7 (6.6)	61.1 (6.6)
Sex (M:F)	18:17	18:16
Height (m)	1.69 (0.08)	1.69 (0.10)
Mass (kg)	71.8 (13.7)*	86.8 (14.9)*
BMI (kg/m^2)	25.1 (3.7)*	30.2 (4.5)*
Walking Velocity (m/s)	1.16 (0.10)*	1.09 (0.10)*
KOS giving way score	[33]5 - [2]4	[10]5 - [8]4 - [7]3 - [8]2 - [1]1
KOOS		
Symptoms (n/100)	98 (4)*	59 (14)*
Pain (n/100)	99 (3)*	65 (16)*
Activities of Daily Living (n/100)	100 (1)*	69 (19)*
Quality of Life (n/100)	97 (5)*	47 (18)*

BMI – Body Mass Index.

KOS – Knee Outcome Survey

KOOS – Knee Osteoarthritis Outcome Score.

* Indicates a significant difference between groups $p < 0.5$

Individuals with knee OA had a greater mass (p < 0.001), greater BMI (p < 0.001), and walked at a slower self-selected speed (p = 0.016). There were no between group differences in age (p = 0.814). Leg stiffness and equation components are included in Table 5.2. Appendix B includes representative figures of both the ground reaction forces vs. percent stance phase and calculated leg length vs. percent stance phase.

Table 5.2: Mean (standard deviation) leg stiffness measurements and corresponding equation components for individuals with knee OA and ASYM individuals at baseline, T0 and T1.

	ASYM			OA		
	Baseline	T0	T1	Baseline	T0	T1
Leg Stiffness (Dimensionless)	7.03 (1.27)	7.04 (1.32)	7.61 (1.48)	6.41 (0.72)	6.41 (0.64)	7.10 (1.43)
Maximum Ground Reaction Force (N) (Normalized to Weight in N)	1.12 (0.09)	1.12 (0.10)	1.16 (0.10)	1.07 (0.06)	1.07 (0.06)	1.12 (0.08)
Initial Leg Length (L_o) (m)	0.992 (0.049)	0.992 (0.049)	0.991 (0.049)	0.991 (0.058)	0.992 (0.058)	0.991 (0.060)
Minimum Leg Length (L_{min}) (m)	0.831 (0.050)	0.830 (0.051)	0.835 (0.050)	0.824 (0.053)	0.825 (0.052)	0.830 (0.051)
Change in Leg Length (L_0-L_{min}/L_0)	0.163 (0.021)	0.163 (0.022)	0.157 (0.027)	0.168 (0.015)	0.169 (0.016)	0.163 (0.022)

5.4.1 Mixed Model Analysis of Variance

Mauchly's test of sphericity was violated within the data set (p = <0.001) so a Greeshouse-Geisser correction was utilized (degrees of freedom = 1.174). A significant main time effect was identified for repeated measures of leg stiffness with a medium to large effect size (p = <0.001, η^2 = 0.294, d = 0.641). There was not a significant time*group interaction (p = 0.659, η^2 = 0.004, d = 0.063). A significant between subject effect was identified between individuals with knee OA and ASYM individuals when measuring leg stiffness with a small to medium effect size (p = 0.03, η^2 0.068, d = 0.268).

5.4.2 Post-Hoc Testing

Post-hoc dependent t-tests were performed for both individuals with knee OA and ASYM individuals comparing baseline and T0 to determine a reference value for the leg stiffness calculations. Figure 5.1 depicts the changes in leg stiffness at each timepoint for both individuals with knee OA and ASYM individuals. No significant differences between baseline and T0 leg stiffness values were identified in both individuals with knee OA (p = 0.904, d = 0.021) and ASYM individuals (p = 0.919, d = -0.017). Post-hoc dependent t-tests were performed to determine specific differences in leg stiffness measurements within the groups in response to the perturbation. Leg stiffness increased at T1 compared to T0 for both individuals with knee OA (p = 0.001, d = -0.563) and ASYM individuals (p = <0.001, d = -0.884).

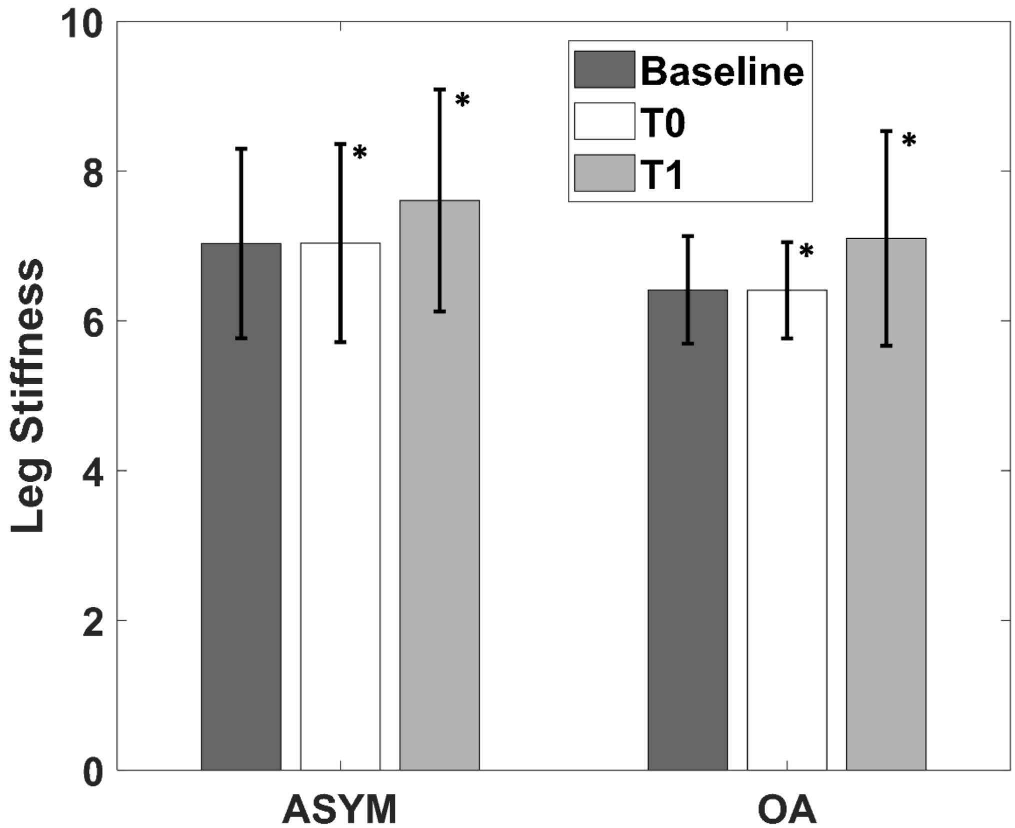

Figure 5.1: Leg Stiffness measurements at baseline, T0, and T1 for ASYM individuals and individuals with knee OA. The star represents a significant increase in leg stiffness from T0 to T1 for both ASYM individuals and individuals with knee OA.

5.5 Discussion

This study first aimed to determine reference values for the leg stiffness calculations when using a dual-belt instrumented treadmill during stance. Additionally, the study aimed to determine whether leg stiffness was altered in response to an unexpected 3 cm medial walking surface translation during stance for individuals with knee OA compared to ASYM individuals. The hypotheses were that both groups would increase their leg stiffness in response to the unexpected medial surface translations.

Additionally, individuals with knee OA would have a lower leg stiffness than ASYM individuals, indicating that individuals with knee OA would walk with a decreased ability to resist deformation of the lower limb which could potentially lead to instability. The leg stiffness measurement was found to calculate a reproducible reference value. Study results supported the proposed hypotheses whereby both groups increased their lower limb leg stiffness in response to the 3 cm medial perturbation, and individuals with knee OA did have an overall lower leg stiffness compared to ASYM individuals during normal walking.

Detailed in Table 5.1, similarities existed between groups for age, sex distribution, and height. Individuals with knee OA additionally replicated characteristic trends associated with knee OA, and commonly reported in the literature, where they demonstrated a significantly a slower walking velocity, higher mass and BMI, and lower KOOS scores compared to ASYM individuals (81,85), with more self-reported episodes of giving way of the knee joint which affected their daily activity as determined by the KOS. While a slower walking velocity was identified, the difference between individuals with knee OA and ASYM individuals was less than the minimal detectable change (0.09 m/s) indicating the difference in walking velocity could likely be due to chance variation (88) and not an influence on study results. With similar characteristics identified, the selected knee OA cohort has been confirmed to be characteristic of individuals with mild to moderate knee OA.

A known standard of reference for leg stiffness has not been identified within the literature. Leg stiffness value discrepancies exist as computation methodology has been shown to produce different values depending on how leg stiffness is calculated (139,140).

Therefore, a reference value using the outlined leg stiffness calculation was first established when using a dual-belt instrumented treadmill before proceeding to the analysis of the effects of a 3 cm medial perturbation. To ensure consistent reference leg stiffness measurements were calculated, baseline measurements after 6 minutes of normal walking was compared to T0. ASYM individuals demonstrated a leg stiffness of approximately 7.03 at both baseline and T0 whereas individuals with knee OA demonstrated a lower leg stiffness of approximately 6.41 at both baseline and T0 (Table 5.2). No significant differences in leg stiffness were identified when comparing baseline and T0 leg stiffness (Figure 5.1) in both individuals with knee OA ($p = 0.904$, $d = 0.021$) and ASYM individuals ($p = 0.919$, $d = -0.017$), indicating that the proposed leg stiffness computation can be used to identify possible changes in leg stiffness in response to a surface translation. Additionally, no identified significant differences between the baseline and T0 leg stiffness measurements potentially indicates that the perturbation does not have a lasting effect on leg stiffness and both groups are able to adapt a "normal" measure of leg stiffness (168) during and following the 24-minute perturbation protocol.

A significant time effect was identified when comparing leg stiffness at different time intervals using a mixed model ANOVA. Dependent t-tests identified that both individuals with knee OA and ASYM individuals significantly increased their leg stiffness in response to a 3 cm medial perturbation (Table 5.2, Figure 5.1). An increase in leg stiffness has previously been indicated as a necessary biomechanical adaptation to maintain stability while accepting body weight (78,138). Additionally, leg stiffness has been proposed to be maintained by two contributing factors – either through an increase in skeletal component by decreasing the flexion of the lower limb joints, or by increasing the muscular component by increasing muscle activity and resulting joint moments (78,167). Previous perturbation literature has demonstrated a significant increase in muscle activity with no significant kinematic changes in response to a 3 cm perturbation (81). Therefore, current results align with previous findings whereby leg stiffness is increased in response to a perturbation via a resultant increase in muscle activity to maintain stability during weight acceptance. This could indicate that during normal walking, all individuals potentially have a lower active muscle stiffness (131,167) and experience a greater metabolic cost (72) in response to a 3 cm medial perturbation.

A significant between group effect was also identified when comparing leg stiffness at different time intervals between individuals with knee OA and ASYM individuals using a mixed model ANOVA. Examining the components used to calculate leg stiffness, it appears that ASYM individuals had a larger peak vGRF compared to individuals with knee OA and minimal differences in change in leg length, indicating the difference in vGRFs drives the changes seen in leg stiffness in this sample. Higher peak vGRFs have previously been identified as a result of increased walking speed; therefore, decreasing leg stiffness at slower walking speeds (77,78) in individuals with knee OA. Further, an increase in leg stiffness has been demonstrated to indicate an increase in functional performance during tasks of jumping (131,138,167). The lower leg stiffness observed in individuals with knee OA compared to ASYM individuals could potentially suggest a decrease in functional performance during controlled walking and in response to the perturbation. Additionally, the decrease in leg stiffness could also relate to a lack of skeletal component available to maintain stiffness in individuals with knee OA. While individuals with knee OA demonstrated significantly lower leg stiffness values, they were able to proportionally increase their leg stiffness in response to the perturbation. This could indicate that in response to the 3 cm medial perturbation, individuals with knee OA are able to increase their leg stiffness sufficiently to maintain functional performance and successfully respond to the perturbation despite walking with a lower leg stiffness. Therefore, while individuals with knee OA are presenting with limitations and perceived instability (20,22), their lower limb is able to successfully perform compensatory mechanisms to maintain stability through an increase in leg stiffness similar to ASYM individuals. This finding further supports that gait perturbation training may be feasible in knee OA rehabilitation (85) to improve functional performance.

The results in this study must be interpreted considering certain limitations. Individuals were included in data analysis if they completed at least 2/3 successful 3 cm medial perturbations. By not including individuals who only completed one successful 3 cm medial perturbations, more significant changes in leg stiffness might be missed that represent a more unstable group of individuals. These individuals potentially would not be able to increase their leg stiffness in response to the perturbation due to further advanced instability and a lack of ability to efficiently compensate. Additionally, while leg stiffness was measured, individual joint stiffness measurements were not performed. The literature has conflicting opinions over the relationship between joint stiffness and leg stiffness whereby some have shown that leg stiffness is not determined by joint stiffness (77) and others believe individual joint stiffness directly influences leg stiffness (79). An investigation into hip, knee, and ankle joint stiffness in response to a 3 cm medial perturbation could provide more insight into how the lower limb is increasing stiffness to maintain stability. Further, by using the pelvis to calculate leg length, an accurate measurement of varying leg length might not have been obtained as opposed to measuring from the greater trochanter. The pelvis was selected so contributions of the hip to leg stiffness was included in this model. Additionally, stiffness associated with the pelvis could have been introduced into the current model as motion was measured. While differences in leg length could have changed the magnitude of leg stiffness, previous literature has demonstrated the use of the pelvis did not substantially change their conclusions in leg stiffness trends (72). Finally, walking velocity has been shown to influence leg stiffness (77,78). By controlling walking velocity across both groups, additional changes in leg stiffness may be identified as a direct result of knee OA and could provide insight into their functional performance when responding to perturbations.

5.6 Conclusion

In summary, reference values for calculated leg stiffness were obtained when using a dual-belt instrumented treadmill. Both individuals with knee OA and ASYM individuals responded to a 3 cm medial perturbation by increasing their leg stiffness directly after the perturbation. By comparison with baseline measurements, the leg stiffness calculation used was able to produce a standard of reference and indicated that leg stiffness returned to a baseline measurement at some time after the perturbation. Therefore, an increase in leg stiffness was not maintained during and following 24 minutes of perturbed walking. Finally, individuals with knee OA were found to have a significantly lower leg stiffness compared to ASYM individuals, but both groups followed a pattern of increasing their leg stiffness after the perturbation. It is proposed that this was done so via an increase in muscular control in response to the perturbation and individuals with knee OA can increase their functional performance when needed similarly to ASYM individuals. Additionally, individuals with knee OA demonstrate a lower leg stiffness potentially suggesting they are lacking a contribution of skeletal stiffness which could contribute to episodes of instability.

Chapter 6 – Discussion

Knee OA has been a leading topic of research over many years due to its highly prevalent occurrence worldwide as well as significant impact it has on those suffering in terms of physical limitations, associated pain, and resultant comorbidities. Within knee OA literature, the knee joint specifically has been largely studied through gait analysis methodologies to understand the knee joint impairments and limitations with the activity of walking. Changes in knee kinematics, kinetics, and muscle activation patterns have been found. Additionally, great strides are being made in classifying knee OA in a controlled walking environment, but a disconnect in reported findings arise when an individual moves into a real-world scenario where unpredictable walking conditions are present, and an individual must respond to their surroundings. While studies of individuals with knee OA in both controlled and unexpected walking environments commonly report the effects on the knee, an integrated synergy of the entire lower limb is required to support walking. Research is limited or non-existent when examining the effect of knee OA on the entire lower limb, specifically when performing gait perturbations. To better understand the effects of knee OA on the lower limb, the main purpose of this thesis was to understand how ASYM individuals and individuals with knee OA respond to unexpected surface translations as characterized by the response of the lower limb. Two metrics that can characterize lower limb responses include the support moment and leg stiffness, but these metrics have not been used to characterize the response of the lower limb to a surface perturbation in individuals with knee OA.

6.1 Objective 1

The first objective of this thesis (Chapter 4) was to determine whether the peak support moment and percent contributions from the hip, knee, and ankle were altered in response to an unexpected 3 cm medial walking surface translation during stance for ASYM individuals and individuals with knee OA. Proposed hypotheses were partially supported by results. Both individuals with knee OA and ASYM individuals were found to increase their peak support moment in response to the 3 cm medial perturbation and did so by using a similar control strategy. Both groups reorganized the contributions of the major lower limb joints at T1 where the knee and hip contributions were significantly reduced, and the ankle contribution was significantly increased. Study results partially support the proposed hypotheses whereby both groups increased their peak support moment in response to the perturbation, but both groups were found to respond using a similar control strategy. This would suggest that while individuals with knee OA report more episodes of buckling and giving away (Table 4.1) (40,55,58), the lower limb is able to compensate and maintain stability in response to a perturbation.

Despite previous perturbation studies reporting that individuals with knee OA were not found to biomechanically alter their gait in response to the perturbations at the level of the knee (81,86,87), present findings demonstrate that when the lower limb is analyzed, biomechanical differences are identified. These changes in support moment and percent joint moment contributions are supported by previously identified elevated and prolonged muscle activation patterns as a direct response to a perturbation greater than 2 cm (81,86,87). Overall, individuals with knee OA and ASYM individuals continue to demonstrate similar responses to a surface translation indicating individuals with knee OA can maintain stability when challenged through perturbation walking.

6.2 Objective 2

The second objective of this thesis (Chapter 5) was to perform an exploratory study to determine reference values for leg stiffness in individuals with knee OA and ASYM individuals using a dual-belted instrumented treadmill. Additionally, to determine whether leg stiffness was altered immediately after the application of an unexpected 3 cm medial walking surface translation during stance for individuals with knee OA compared to ASYM individuals. The proposed hypotheses were supported by results. The leg stiffness calculation used was able to produce a standard of reference and indicated that leg stiffness returned to a baseline measurement at some time after the perturbation as baseline and T0 measurements did not demonstrate significant differences for either group. In response to a 3 cm medial perturbation, both individuals with knee OA and ASYM individuals increased their leg stiffness directly after the perturbation. Finally, individuals with knee OA were found to have a significantly lower leg stiffness compared to ASYM individuals. Overall it can be concluded that while individuals with knee OA are demonstrating a lower leg stiffness measurement, indicating a reduced ability to resist deformation (131) and could potentially lead to instability, they are able to increase performance in response to a perturbation through an increase in leg stiffness.

Despite previous literature not reporting a standard of reference of leg stiffness (139,140), conclusions were able to be made within this study regarding the control of the musculoskeletal system on the lower limb (78). Leg stiffness has been shown to be influenced by walking speed (78), peak vGRF (77), and muscular control (167). These factors were not controlled in this exploratory study and results should be reviewed with this consideration when comparing absolute values. Overall, individuals with knee OA and ASYM individuals again demonstrated similar responses to a surface translation indicating individuals with knee OA can maintain stability when challenged through perturbation walking.

6.3 Discussion

The support moment investigation proposed in objective 1 (Chapter 4) suggests that both individuals with knee OA and ASYM individuals required more support from the lower limb to maintain walking immediately after experiencing a 3 cm medial perturbation. The greater peak support moment found in both groups would suggest a strategy to resist gravity, prevent limb collapse, and perhaps, maintain stability was adopted in response to the walking perturbation in the current study (158). Additionally, an increase in support moment would suggest an increased load is being placed on the lower limb in response to the surface translation, but individuals with knee OA have been found to tolerate the increased load without an increase in reported pain (85), further emphasizing the ability of the lower limb to maintain stability while not increasing the mechanical load at the knee joint. Both individuals with knee OA and ASYM individuals were found to significantly decrease the hip and knee contributions to the peak support moment while increasing the ankle contribution from T0 to T1. Therefore, individuals with knee OA and ASYM individuals were found to respond in a similar way to the surface translation as previously reported (81,83,85,86). Further, it is proposed that the knee joint may not play a major role in maintaining support compared to the ankle and hip in response to the medial perturbation. Both groups significantly decreased their knee joint contributions to a minimal threshold which could explain why individuals with knee OA were able to successfully perform throughout the perturbation protocol. Alternatively, the ankle was shown to dominate support which is proposed to be the result of a strategy implemented to control the centre of mass that is further displaced by a medial perturbation and generating a resultant dominating ankle joint moment (165). Overall, a greater demand was put on the ankle in response to the walking perturbation.

The leg stiffness investigation proposed in objective 2 (Chapter 5) suggests that both individuals with knee OA and ASYM individuals responded with an increase in leg stiffness immediately after experiencing a 3 cm medial perturbation. A standard reference value for leg stiffness for individuals with knee OA and ASYM individuals was established and shown to be consistent when comparing baseline and T0 measurements. No identified significant differences between the baseline and T0 leg stiffness measurements potentially indicates that the perturbation does not have a lasting result on leg stiffness and both groups are able to adapt a "normal" measure of leg stiffness (168) following the 24-minute perturbation protocol. Both groups responded to the surface translation with an increase in leg stiffness at T1. Previous perturbation literature has demonstrated a significant increase in muscle activity with no significant kinematic changes in response to a 3 cm perturbation (81). Therefore, current results align with previous findings whereby leg stiffness could be increased in response to the perturbation via the resultant increase in muscle activity to maintain stability during weight acceptance. While both groups followed a similar pattern of increasing leg stiffness, individuals with knee OA had an overall lower leg stiffness. This could indicate that individuals with knee OA potentially have a lower active muscle stiffness (131,167) –

resulting in reported instability – but are able to increase their functional performance in response to the perturbation.

The investigation into both the support moment and leg stiffness additionally demonstrated similarities in results. Individuals with knee OA demonstrated both a lower magnitude of support moment and lower leg stiffness than ASYM individuals. This could potentially be attributed to more self-reported instances of instability and related to previously reported results where knee OA limits an individual's function, both during normal walking (20), and in response to the perturbation. Additionally, the peak vGRF was identified to control to magnitude of leg stiffness in the current investigation. The peak vGRF was identified in the early half of stance (approximately around 15 to 25 % of stance phase), which was comparable to the position that the peak support moment was identified. The support moment was then sustained at a higher magnitude through stance phase at T1. This could suggest that in response to a perturbation, the entire lower limb is responding during the loading response phase of gait (118) to increase both support and stiffness.

The primary focus of this thesis was to investigate how individuals with MOA and ASYM individuals respond to unexpected 3cm medial surface translations during gait, characterized by the response of the entire lower limb during the stride following the perturbation (response stride). While previous literature did not identify significant changes in biomechanical differences in response to the perturbation at the knee, an analysis of both the support moment and leg stiffness have provided insight into the cooperative nature of the lower limb and overall suggests that the lower limb joints – hip, knee, and ankle – work in unison to respond to walking surface translations. These responses are similar in individuals with MOA and ASYM individuals indicating that individuals with MOA can adapt to environmental conditions despite limitations at the knee joint through compensatory mechanisms of the lower limb to increase both support and stiffness.

6.4 Limitations

The results in this thesis must be interpreted considering certain limitations. As the same study participants were used for the data analyses in both Chapter 4 and 5, participant selection limitations applied to both studies. Individuals were filtered on the premise that they were able to complete at least 2/3 successful 3 cm medial surface perturbations. Every participant was able to complete the perturbation testing, however crossing onto the other plate or grabbing the handrails in response to the perturbation was deemed an unsuccessful trial. Theoretically, more failed attempts at completing the perturbation could indicate that the individual is more unstable in response to a 3 cm medial perturbation. By removing all individuals who only completed one successful trial or did not successfully complete any trials, we are potentially missing changes in control patterns of the lower limb, presented as a change in support moment / joint moment contributions or leg stiffness, that could be utilized in a more unstable group. In regard to the support moment and joint moment contributions, by removing trials where a person was unsuccessful could be inadvertently manipulating the data set to show a more similar pattern in movement between individuals with knee OA and ASYM individuals. In terms of leg stiffness, these individuals potentially would not be able to increase their leg stiffness in response to the perturbation due to further advanced instability and a lack of ability to efficiently compensate. While it is assumed that individuals with knee OA would have fewer successful trials compared to ASYM individuals, the current perturbation protocol has demonstrated that there were a similar number of unsuccessful trials for both groups (81). Alternatively, Schrijvers et. al, has shown that individuals who self report knee instability respond differently to perturbations (86). Within the current sample, almost half the individuals with knee OA reported moments of instability affecting their daily activities whereas no ASYM individuals reported episodes of instability affecting their daily activities. Therefore, further exploration is warranted to examine how individuals with knee OA who self-reported knee instability could elicit further changes in the lower limb that does not align with how ASYM individual respond to walking perturbations.

Another present limitation in both analyses is walking velocity was not controlled for within this sample. An increase in walking velocity has been found to demonstrate changes in the support moment and percent joint moment contributions (69) as well as elicit changes in foot placement during walking (165). Additionally, walking velocity has been shown to influence leg stiffness (77,78). Self-selected walking velocity and the impact this may have on the lower limb in response to walking perturbations requires further study in older adults and individuals with knee OA. While walking speed may have a between group influence on lower limb measurement magnitudes, comparing the response between T0 and T1 could continue to produce similar results as the walking velocity was consistent for each participant throughout the perturbation protocol. Additionally, even though a slower walking velocity was identified, the difference between individuals with knee OA and ASYM individuals was less than the minimal detectable change indicating the difference in walking velocity could likely be due to chance variation (88) and not an influence on study results.

Finally, while leg stiffness was measured, individual joint stiffness measurements were not performed. The literature has conflicting opinions over the relationship between joint stiffness and leg stiffness whereby some have shown that leg stiffness is not determined by joint stiffness (77) and others believe individual joint stiffness directly influences leg stiffness (79). An investigation into hip, knee, and ankle joint stiffness in response to a 3 cm medial perturbation could provide more insight into how the lower limb is increasing stiffness to maintain stability.

6.5 Future Directions

Numerous future directions could be explored following the results of this thesis. Chapter 4 examined the support moment in response a 3cm medial surface perturbation using a dual-belt instrumented treadmill. While the support moment has been found to be less variable than individual joint moments and more reproducible when comparing across the literature (156,157), a reliability study of the support moment and percent joint moment contributions would be useful to further strengthen conclusions made in this thesis. A reliability study also has the possibility of investigating the large standard deviations present in the joint moment contributions. Chapter 5 worked to explore the leg stiffness calculation and develop a standard reference value of leg stiffness. Similarly, a reliability study of leg stiffness would be useful to further support the reproducibility of the measurement, confirm an accurate standard of reference has been established when using a dual-belt instrumented treadmill, and strengthen the conclusion that both individuals with knee OA and ASYM individuals are returning to baseline leg stiffness at some time post perturbation.

Additionally, the analyses performed for both the support moment and leg stiffness identify walking velocity as a possible influence on study results. Alternate statistical analysis could be performed on each data set controlling for walking velocity such a factorial ANOVA or an analysis of covariance. Further, both studies also identified the possibility of varying results if individuals with knee OA who self-reported knee instability was used. From the current study sample of individuals with knee OA, 16 out of 34 individuals reported that episodes of buckling or giving away (classified as instability) affected their daily living (Table 4.1, Table 5.1). With almost half the individuals with knee OA self-reporting instability, alternative or more drastic differences in either support moment, percent joint moment contributions, or leg stiffness could be identified in individuals with knee OA who self-report knee instability. Comparing individuals with knee OA who self-report knee instability to individuals with knee OA who do not report instability or ASYM individuals could help to better classify the response of the lower limb. Finally, further analysis could also be used to examine other influencing factors such as the degree of pain, the stage of knee OA, and a sex analysis.

Within Chapter 5, the literature was shown to have conflicting opinions over the relationship between joint stiffness and leg stiffness whereby some have shown that leg stiffness is not determined by joint stiffness (77) and others believe individual joint stiffness directly influences leg stiffness (79). An investigation into the relationship between individual joint stiffness measures and leg stiffness could be useful to further understand the mechanisms by which the lower limb is increasing stiffness in response to the medial perturbation. Additionally, an analysis of joint stiffness could further support the compensatory mechanism used in response to surface perturbations.

Finally, a long-term study using perturbed walking as a rehabilitation regime in individuals with knee OA could be used to study the effects of perturbed walking over time. Chapter 4 and 5, as well as previous literature, has suggested that individuals with knee OA tolerate the perturbation protocol without an increase in pain and return to baseline measurements following the perturbation. Therefore, gait perturbation training may be feasible in knee OA rehabilitation (85) to improve functional performance in day-to-day living. A long-term study using the perturbation protocol would be useful to test the proposed rehabilitation benefits.

6.6 Concluding Remarks

The main aim of this thesis was to determine how individuals with moderate knee OA and ASYM individuals respond to unexpected 3cm medial surface translations during gait, characterized by the response of the entire lower limb following the perturbation. Individuals with knee OA were found to respond similarly to ASYM individuals in both measurements of the support moment and leg stiffness. Both groups required more support in response to the perturbation and utilized a reorganized control strategy with dominating ankle contribution. Both groups additionally required more leg stiffness to maintain stability in response to the perturbation, with individuals with knee OA demonstrating a lower leg stiffness when compared to ASYM individuals. By increasing their leg stiffness measurement at T1, both groups demonstrated an increased functional performance in response to the perturbation. Therefore, while individuals with knee OA are presenting with limitations and perceived instability (20,22), their lower limb is able to successfully perform compensatory mechanisms to maintain stability through an increase in both the support moment and leg stiffness similar to ASYM individuals in response to a medial perturbation. These findings support that gait perturbation training may be feasible in knee OA rehabilitation (85) to improve functional performance.

References

1. Dreinhöfer K, Stucki G, Ewert T, Huber E, Ebenbichler G, Gutenbrunner C, et al. ICF Core Sets for osteoarthritis. J Rehabil Med Suppl. 2004;(44):75–80.

2. Panjabi MM. The stabilizing system of the spine: Part I. function, dysfunction, adaptation, and enhancement. Vol. 5, Journal of Spinal Disorders. 1992. p. 383–9.

3. Pirker W, Katzenschlager R. Gait disorders in adults and the elderly: A clinical guide. Wien Klin Wochenschr. 2017;129(3–4):81–95.

4. Felson DT. Osteoarthritis as a disease of mechanics. Vol. 21, Osteoarthritis and Cartilage. 2013. p. 10–5.

5. Lane NE, Brandt K, Hawker G, Peeva E, Schreyer E, Tsuji W, et al. OARSI-FDA initiative: Defining the disease state of osteoarthritis. Osteoarthr Cartil. 2011;19(5):478–82.

6. 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.

7. Information CI for H. Hip and knee replacement in Canada: CJRR annual report CIHI. Vol. 2021. 2022. Available from: https://www.cihi.ca/en/hip-and-knee-replacements-in-canada-cjrr-annual-report.

8. CJRR. Canadian Joint Replacement Registry. 2021. 1–63 p. Available from: https://se-cure.cihi.ca/free_products/CJRR_2015_Annual_Report_EN.pdf.

9. Gupta S, Hawker GA, Laporte A, Croxford R, Coyte PC. The economic burden of disabling hip and knee osteoarthritis (OA) from the perspective of individuals living with this condition. Rheumatology. 2005;44:1531–7.

10. 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):1233–41.

11. Hunter DJ. Lower extremity osteoarthritis management needs a paradigm shift. Vol. 45, British Journal of Sports Medicine. 2011. p. 283–8.

12. Stewart HL, Kawcak CE. The importance of subchondral bone in the pathophysiology of osteoarthritis. Front Vet Sci. 2018;5:1–9.

13. Wilson DR, McWalter EJ, Johnston JD. The Measurement of Joint Mechanics and Their Role in Osteoarthritis Genesis and Progression. Vol. 39, Rheumatic Disease Clinics of North America. 2013. p. 21–44.

14. Brandt KD, Dieppe P, Radin E. Etiopathogenesis of Osteoarthritis. Med Clin North Am. 2009;93(1):1–24.

15. Eckstein F, Wirth W, Hudelmaier MI, Maschek S, Hitzl W, Wyman BT, et al. Relationship of compartment-specific structural knee status at baseline with change in cartilage morphology: A prospective observational study using data from the osteoarthritis initiative. Arthritis Res Ther. 2009;11(3).

16. Mündermann A, Dyrby CO, D'Lima DD, Colwell CW, Andriacchi TP. In vivo knee loading characteristics during activities of daily living as measured by an instrumented total knee replacement. J Orthop Res. 2008;26(9):1167–72.

17. Schipplein OD, Andriacchi TP. Interaction between active and passive knee stabilizers during level walking. J Orthop Res. 1991;9(1):113–9.

18. Felson DT, Niu J, McClennan C, Sack B, Aliabadi P, Hunter DJ, et al. Knee buckling: Prevalence, risk factors, and associated limitations in function. Ann Intern Med. 2007;147(8):534–40.

19. Sharma L, Chmiel JS, Almagor O, Moisio K, Chang AH, Belisle L, et al. Knee instability and basic and advanced function decline in knee osteoarthritis. Arthritis Care Res. 2015;67(8):1095–102.

20. Fitzgerald GK, Piva SR, Irrgang JJ. Reports of joint instability in knee osteoarthritis: Its prevalence and relationship to physical function. Arthritis Care Res. 2004;51(6):941–6.

21. Van Der Esch M, Knoop J, Van Der Leeden M, Voorneman R, Gerritsen M, Reiding D, et al. Self-reported knee instability and activity limitations in patients with knee osteoarthritis: Results of the Amsterdam osteoarthritis cohort. Clin Rheumatol. 2012;31(10):1505–10.

22. Skou ST, Wrigley T V, Metcalf BR, Hinman RS, Bennell KL. Association of knee confidence with pain, knee instability, muscle strength, and dynamic varus-valgus joint motion in knee osteoarthritis. Arthritis Care Res. 2014;66(5):695–701.

23. Feinglass J, Thompson JA, He XZ, Witt W, Chang RW, Baker DW. Effect of physical activity on functional status among older middle-age adults with arthritis. Arthritis Care Res. 2005;53(6):879–85.

24. Fontaine KR, Haaz S. Risk factors for lack of recent exercise in adults with self-reported, professionally diagnosed arthritis. J Clin Rheumatol. 2006;12(2):66–9.

25. Felson DT. Risk factors for osteoarthritis: Understanding joint vulnerability. Clin Orthop Relat Res. 2004;427(SUPPL.):16–21.

26. Tudor-Locke CE, Myers AM. Methodological considerations for researchers and practitioners using pedometers to measure physical (ambulatory) activity. Res Q Exerc Sport. 2001;72(1):1–12.

27. Gardner PJ, Campagna PD. Pedometers as Measurement Tools and Motivational Devices: New Insights for Researchers and Practitioners. Health Promot Pract. 2011;12(1):55–62.

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.

29. 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 Jul 1;30(6):578–84.

30. 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;45:25–31.

31. 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):365–78.

32. 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):868–76.

33. Zeni JA, Higginson JS. Knee Osteoarthritis Affects the Distribution of Joint Moments During Gait. Knee. 2011;18(3):156–9.

34. Gök H, Ergin S, Yavuzer G. Kinetic and kinematic characteristics of gait in patients with medial knee arthrosis. Acta Orthop Scand. 2002 Dec;73(6):647–52.

35. Bytyqi D, Shabani B, Lustig S, Cheze L, Karahoda Gjurgjeala N, Neyret P. Gait knee kinematic alterations in medial osteoarthritis: Three dimensional assessment. Int Orthop. 2014;38(6):1191–8.

36. Chang AH, Chmiel JS, Moisio KC, Almagor O, Zhang Y, Cahue S, et al. Varus thrust and knee frontal plane dynamic motion in persons with knee osteoarthritis. Osteoarthr Cartil. 2013;21(11):1668–73.

37. Rudolph KS, Schmitt LC, Lewek MD. Age-related changes in strength, joint laxity, and walking patterns: Are they related to knee osteoarthritis? Phys Ther. 20007;87(11):1422–32.

38. Briem K, Snyder-Mackler L. Proximal gait adaptations in medial knee OA. J Orthop Res. 2009;27(1):78–83.

39. Kumar D, Manal KT, Rudolph KS. Knee joint loading during gait in healthy controls and individuals with knee osteoarthritis. Osteoarthr Cartil. 2013;21(2):298–305.

40. 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):44–9.

41. 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):505–11.

42. Kaufman KR, Hughes C, Morrey BF, Morrey M, An KN. Gait characteristics of patients with knee osteoarthritis. J Biomech. 2001;34(7):907–15.

43. 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):332–41.

44. Heiden TL, Lloyd DG, Ackland TR. Knee joint kinematics, kinetics and muscle co-contraction in knee osteoarthritis patient gait. Clin Biomech. 2009;24(10):833–41.

45. Boyer KA, Hafer JF. Gait mechanics contribute to exercise induced pain flares in knee osteoarthritis. BMC Musculoskelet Disord. 2019;20(1):1–10.

46. Favre J, Erhart-Hledik JC, Andriacchi TP. Age-related differences in sagittal-plane knee function at heel-strike of walking are increased in osteoarthritic patients. Osteoarthr Cartil. 2014;22(3):464–71.

47. Henriksen M, Graven-Nielsen T, Aaboe J, Andriacchi TP, Bliddal H. Gait changes in patients with knee osteoarthritis are replicated by experimental knee pain. Arthritis Care Res. 2010;62(4):501–9.

48. 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):1004–14.

49. 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):704–11.

50. Neumann DA. Kinesiology of Walking. In: Kinesiology of the Musculoskeletal System: Foundations for Physical Rehabilitation. DA N Ed. St. Louis, Missouri: Mosby, Inc.; 2002. p. 523–69.

51. Moore K, Dalley A, Agur A. Clinically Oriented Anatomy. 8th ed. Philadelphia (USA): Wolters Kluwer; 2018.

52. 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.

53. Dixon SJ, Hinman RS, Creaby MW, Kemp G, Crossley KM. Knee joint stiffness during walking in knee osteoarthritis. Vol. 62, Arthritis Care and Research. 2010. p. 38–44.

54. 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):745–51.

55. Schmitt LC, Rudolph KS. Influences on knee movement strategies during walking in persons with medial knee osteoarthritis. Arthritis Care Res. 2007;57(6):1018–26.

56. 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):186–93.

57. 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):1859–64.

58. Farrokhi S, Tashman S, Gil AB, Klatt BA, Fitzgerald GK. Are the kinematics of the knee joint altered during the loading response phase of gait in individuals with concurrent knee osteoarthritis and complaints of joint instability? A dynamic stereo X-ray study. Clin Biomech. 2012;27(4):384–9.

59. 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):1754–61.

60. 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):1661–70.

61. Creaby MW. It's not all about the knee adduction moment: The role of the knee flexion moment in medial knee joint loading. Osteoarthr Cartil. 2015;23(7):1038–40.

62. Baliunas AJ, Hurwitz DE, Ryals AB, Karrar A, Case JP, Block JA, et al. Increased knee joint loads during walking are present in subjects with knee osteoarthritis. Osteoarthr Cartil. 2002;10(7):573–9.

63. Hurwitz DE, Ryals AB, Case JP, Block JA, Andriacchi TP. The knee adduction moment during gait in subjects with knee osteoarthritis is more closely correlated with static alignment than radiographic disease severity, toe out angle and pain. J Orthop Res. 2002;20(1):101–7.

64. 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):617–22.

65. McGibbon CA, Krebs DE. Compensatory gait mechanics in patients with unilateral knee arthritis. J Rheumatol. 2002;29(11):2410–9.

66. Winter DA. Overall principle of lower limb support during stance phase of gait. J Biomech. 1980;13(11):923–7.

67. Sloot LH, Van der Krogt MM. Interpreting joint moments and powers in gait. In: Handbook of Human Motion. 2018. p. 625–43.

68. Fukui T, Ueda Y, Kamijo F. Ankle, knee, and hip joint contribution to body support during gait. J Phys Ther Sci. 2016;28(10):2834–7.

69. Zeni JA, Higginson JS. Knee osteoarthritis affects the distribution of joint moments during gait. Knee. 2011;18(3):156–9.

70. 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.

71. 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):351–9.

72. Silder A, Besier T, Delp SL. Running with a load increases leg stiffness. J Biomech. 2015;48(6):1003–8.

73. Padua DA, Garcia CR, Arnold BL, Granata KP. Gender differences in leg stiffness and stiffness recruitment strategy during two-legged hopping. J Mot Behav. 2005;37(2):111–26.

74. Farley CT, Morgenroth DC. Leg stiffness primarily depends on ankle stiffness during human hopping. J Biomech. 1999;32(3):267–73.

75. Arampatzis A, Schade F, Walsh M, Brüggemann GP. Influence of leg stiffness and its effect on myodynamic jumping performance. J Electromyogr Kinesiol. 2001;11(5):355–64.

76. Oliver JL, Smith PM. Neural control of leg stiffness during hopping in boys and men. J Electromyogr Kinesiol. 2010;20(5):973–9.

77. Akl AR, Baca A, Richards J, Conceição F. Leg and lower limb dynamic joint stiffness during different walking speeds in healthy adults. Gait Posture. 2020;82:294–300.

78. Wei IP, Hsu WC, Chien HL, Chang CF, Liu YH, Ho TJ, et al. Leg and joint stiffness in patients with bilateral medial knee osteoarthritis during level walking. J Mech. 2009;25(3):279–87.

79. Gustafson JA, Gorman S, Fitzgerald GK, Farrokhi S. Alterations in walking knee joint stiffness in individuals with knee osteoarthritis and self-reported knee instability. Gait Posture. 2016;43:210–5.

80. 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):372–8.

81. Baker M, Stanish W, Rutherford D. Walking challenges in moderate knee osteoarthritis: A biomechanical and neuromuscular response to medial walkway surface translations. Hum Mov Sci. 2019 Dec 1;68.

82. Rutherford D, Baker M, Urquhart N, Stanish W. The effect of a frontal plane gait perturbation bout on knee biomechanics and muscle activation in older adults and individuals with knee osteoarthritis. Clin Biomech. 2022;92:105574.

83. Kumar D, Swanik C, Reisman DS, Rudolph KS. Individuals with medial knee osteoarthritis show neuromuscular adaptation when perturbed during walking despite functional and structural impairments. J Appl Physiol. 2014;116(1):13–23.

84. Schmitt LC, Rudolph KS. Muscle stabilization strategies in people with medial knee osteoarthritis: The effect of instability. J Orthop Res. 2008;26(9):1180–5.

85. Rutherford D, Baker M, Urquhart N, Stanish W. The effect of a frontal plane gait perturbation bout on knee biomechanics and muscle activation in older adults and individuals with knee osteoarthritis. Clin Biomech. 2022;92:105574.

86. Schrijvers JC, van den Noort JC, van der Esch M, Harlaar J. Neuromechanical assessment of knee joint instability during perturbed gait in patients with knee osteoarthritis. J Biomech. 2021;118:110325.

87. Rutherford DJ, Baker M, Stanish B. Muscle activation responses to medial and lateral walkway perturbations during gait in individuals with moderate knee osteoarthritis. Osteoarthr Cartil. 2016;24:S115–6.

88. 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 Apr 1;51.

89. Shane Anderson A, Loeser RF. Why is osteoarthritis an age-related disease? Vol. 24, Best Practice and Research: Clinical Rheumatology. 2010. p. 15–26.

90. Kellgren JH, Lawrence JS. RADIOLOGICAL ASSESSMENT OF OSTEO-ARTHROSIS Ann Rheum Dis 1957. Ann rheum Dis. 1956;(3):494–503.

91. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis: Classification of osteoarthritis of the knee. Arthritis Rheum. 1986;29(8):1039–49.

92. Altman RD, Fries JF, Bloch DA, Carstens J, Derek Mb TC, Genant H, et al. Radiographic assessment of progression in osteoarthritis. Arthritis Rheum. 1987;30(11):1214–25.

93. Felson DT, Niu J, Guermazi A, Sack B, Aliabadi P. Defining radiographic incidence and progression of knee osteoarthritis: Suggested modifications of the Kellgren and Lawrence scale. Vol. 70, Annals of the Rheumatic Diseases. 2011. p. 1884–6.

94. Schiphof D, Boers M, Bierma-Zeinstra SMA. Differences in descriptions of Kellgren and Lawrence grades of knee osteoarthritis. Ann Rheum Dis. 2008;67(7):1034–6.

95. Altman RD, Hochberg M, Murphy WA, Wolfe F, Lequesne M. Atlas of individual radiographic features in osteoarthritis. Vol. 3, Osteoarthritis and Cartilage. 1995. p. 3–70.

96. Bennell KL, Dobson F, Roos EM, Skou ST, Hodges P, Wrigley T V, et al. Influence of biomechanical characteristics on pain and function outcomes from exercise in medial knee osteoarthritis and varus malalignment: Exploratory analyses from a randomized controlled trial. Arthritis Care Res. 2015;67(9):1281–8.

97. Knoop J, Van Der Leeden M, Van Der Esch M, Thorstensson CA, Gerritsen M, Voorneman RE, et al. Association of lower muscle strength with self-reported knee instability in osteoarthritis of the knee: Results from the Amsterdam Osteoarthritis Cohort. Arthritis Care Res. 2012;64(1):38–45.

98. Maly MR, Costigan PA, Olney SJ. Determinants of self-report outcome measures in people with knee osteoarthritis. Arch Phys Med Rehabil. 2006;87(1):96–104.

99. 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.

100. Schofield D, Shrestha R, Percival R, Passey M, Callander E, Kelly S. The personal and national costs of CVD: Impacts on income, taxes, government support payments and GDP due to lost labour force participation. Int J Cardiol. 2013;166(1):68–71.

101. Gignac MAM, Backman CL, Davis AM, Lacaille D, Cao X, Badley EM. Social role participation and the life course in healthy adults and individuals with osteoarthritis: Are we overlooking the impact on the middle-aged? Soc Sci Med. 2013;81:87–93.

102. Bhandari M, Smith J, Miller LE, Block JE. Clinical and economic burden of revision knee arthroplasty. Clin Med Insights Arthritis Musculoskelet Disord. 2012;5:89–94.

103. World Health Organization. International Classification of Functioning, Disability and Health: ICF. World Health Organization; 2001. 1–315 p.

104. King LK, Kendzerska T, Waugh EJ, Hawker GA. Impact of Osteoarthritis on Difficulty Walking: A Population-Based Study. Arthritis Care Res. 2018;70(1):71–9.

105. 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):2835–44.

106. Nagano Y, Naito K, Saho Y, Torii S, Ogata T, Nakazawa K, et al. Association between in vivo knee kinematics during gait and the severity of knee osteoarthritis. Knee. 2012;19(5):628–32.

107. Creaby MW, Hunt MA, Hinman RS, Bennell KL. Sagittal plane joint loading is related to knee flexion in osteoarthritic gait. Clin Biomech. 2013;28(8):916–20.

108. 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):265–71.

109. 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):421–7.

110. Pinto RF, Birmingham TB, Leitch KM, Atkinson HF, Jones IC, Giffin JR. Reliability and validity of knee angles and moments in patients with osteoarthritis using a treadmill-based gait analysis system. Gait Posture. 2020;80:155–61.

111. Maly MR, Costigan PA, Olney SJ. Mechanical factors relate to pain in knee osteoarthritis. Clin Biomech. 2008;23(6):796–805.

112. Mith RLANES, Lexander EUJA, Andriacchi TP, Mündermann A, Smith RL, Alexander EJ, et al. A framework for the in vivo pathomechanics of osteoarthritis at the knee. Ann Biomed Eng. 2004;32(3):447–57.

113. Sharma L, Chang AH, Jackson RD, Nevitt M, Moisio KC, Hochberg M, et al. Varus Thrust and Incident and Progressive Knee Osteoarthritis. Arthritis Rheumatol. 2017;69(11):2136–43.

114. 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):226–37.

115. Szczerbik E, Kalinowska M. The influence of knee marker placement error on evaluation of gait kinematic parameters. Acta Bioeng Biomech. 2011;13(3):43–6.

116. Benoit DL, Ramsey DK, Lamontagne M, Xu L, Wretenberg P, Renström P. In vivo knee kinematics during gait reveals new rotation profiles and smaller translations. Clin Orthop Relat Res. 2007;454(454):81–8.

117. Vaughan C., Davis B., O'Connor J. Dynamics of Human Gait. 2nd Editio. Cape Town, South Africa: Kiboho Publishers; 1992.

118. Debbi EM, Wolf A, Goryachev Y, Rozen N, Haim A. Alterations in Sagittal Plane Knee Kinetics in Knee Osteoarthritis Using a Biomechanical Therapy Device. Ann Biomed Eng. 2015;43(5):1089–97.

119. Wiik AV, Aqil A, Brevadt M, Jones G, Cobb J. Abnormal ground reaction forces lead to a general decline in gait speed in knee osteoarthritis patients. World J Orthop. 2017;8(4):322–8.

120. Schipplein OD, Andriacchi TP. Interaction between active and passive knee stabilizers during level walking. J Orthop Res. 1991;9(1):113–9.

121. Al-Zahrani KS, Bakheit AMO. A study of the gait characteristics of patients with chronic osteoarthritis of the knee. Disabil Rehabil. 2002;24(5):275–80.

122. Chehab EF, Favre J, Erhart-Hledik JC, Andriacchi TP. Baseline knee adduction and flexion moments during walking are both associated with 5year cartilage changes in patients with medial knee osteoarthritis. Osteoarthr Cartil. 2014;22(11):1833–9.

123. Hurwitz DE, Ryals AR, Block JA, Sharma L, Schnitzer TJ, Andriacchi TP. Knee pain and joint loading in subjects with osteoarthritis of the knee. J Orthop Res. 2000;18(4):572–9.

124. Boyer KA, Angst MS, Asay J, Giori NJ, Andriacchi TP. Sensitivity of gait parameters to the effects of anti-inflammatory and opioid treatments in knee osteoarthritis patients. J Orthop Res. 2012;30(7):1118–24.

125. Schnitzer TJ, Popovich JM, Andersson GBJ, Andriacchi TP. Effect of piroxicam on gait in patients with osteoarthritis of the knee. Arthritis Rheum. 1993;36(9):1207–13.

126. 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):612–22.

127. Huang SC, Wei IP, Chien HL, Wang TM, Liu YH, Chen 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.

128. Esrafilian A, Karimi MT, Amiri P, Fatoye F. Performance of subjects with knee osteoarthritis during walking: Differential parameters. Rheumatol Int. 2013;33(7):1753–61.

129. Goldberg SR, Stanhope SJ. Sensitivity of joint moments to changes in walking speed and body-weight-support are interdependent and vary across joints. J Biomech. 2013;46(6):1176–83.

130. Winter DA. Biomechanical motor patterns in normal walking. J Mot Behav. 1983;15(4):302–30.

131. Kaminski TW, Padua DA, Blackburn JT. Muscle Stiffness and Biomechanical Stability. Athl Ther Today. 2016;8(6):45–7.

132. Gustafson JA, Anderton W, Sowa GA, Piva SR, Farrokhi S. Dynamic knee joint stiffness and contralateral knee joint loading during prolonged walking in patients with unilateral knee osteoarthritis. Gait Posture. 2019;68:44–9.

133. Hubley-Kozey CL, Stanish WD, Urquhart N, Ikeda DM, Wilson JLA. Longitudinal changes in knee joint gait mechanics and muscle activation patterns in individuals with medial compartment knee osteoarthritis. Osteoarthr Cartil. 2020;28:S58–9.

134. Pauff SM, Miller SC. Dynamic Knee Joint Stiffness in Subjects with a Progressive Increase in Severity of Knee Osteoarthritis. Bone. 2012;78(2):711–6.

135. Benjamin Chun-Kit Tong. Knee motion variability in patients with knee osteoarthritis: the effect of self-reported instability. Physiol Behav. 2017;176(5):139–48.

136. Fallah Yakhdani HR, Bafghi HA, Meijer OG, Bruijn SM, Dikkenberg N van den, Stibbe AB, et al. Stability and variability of knee kinematics during gait in knee osteoarthritis before and after replacement surgery. Clin Biomech. 2010;25(3):230–6.

137. Farley CT, Houdijk HHP, Van Strien C, Louie M. Mechanism of leg stiffness adjustment for hopping on surfaces of different stiffnesses. J Appl Physiol. 1998;85(3):1044–55.

138. Butler RJ, Crowell HP, Davis IMC. Lower extremity stiffness: Implications for performance and injury. Clin Biomech. 2003;18(6):511–7.

139. Hébert-Losier K, Eriksson A. Leg stiffness measures depend on computational method. J Biomech. 2014;47(1):115–21.

140. Coleman DR, Cannavan D, Horne S, Blazevich AJ. Leg stiffness in human running: Comparison of estimates derived from previously published models to direct kinematic-kinetic measures. J Biomech. 2012;45(11):1987–91.

141. Serpell BG, Ball NB, Scarvell JM, Smith PN. A review of models of vertical, leg, and knee stiffness in adults for running, jumping or hopping tasks. J Sports Sci. 2012;30(13):1347–63.

142. Elkarif V, Kandel L, Rand D, Schwartz I, Greenberg A, Portnoy S. Kinematics following gait perturbation in adults with knee osteoarthritis: Scheduled versus not scheduled for knee arthroplasty. Gait Posture. 2020;81:144–52.

143. Altman RD. Criteria for the classification of osteoarthritis of the knee and hip. Scand J Rheumatol. 1987;16(S65):31–9.

144. Schrijvers JC, van den Noort JC, van der Esch M, Harlaar J. Responses in knee joint muscle activation patterns to different perturbations during gait in healthy subjects. J Electromyogr Kinesiol. 2021;60:102572.

145. Field A. Discovering Statistics Using IBM SPSS Statistics. 5th Editio. Sage Publications, Inc. California: SAGE Publications Inc.; 2018.

146. Jones SR, Carley S, Harrison M. An introduction to power and sample size estimation The importance of power and sample size estimation for study design and analysis. Emerg Med J. 2003;20:453–8.

147. Kang H. Sample size determination and power analysis using the G*Power software. J Educ Eval Health Prof. 2021;18:1–12.

148. Faul F, Erdfelder E, Lang A-G, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods. 2007;39(2):175–91.

149. Collins NJ, Misra D, Felson DT, Crossley KM, Roos EM. Measures of knee function: International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, Knee Injury and Osteoarthritis Outcome Score (KOOS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Knee Ou. Arthritis Care Res. 2011;63(SUPPL. 11):S208–28.

150. Sinaiskii BN, Pogrebnyak AD, Ishchenko II. The influence of test temperature on the fatigue strength of ZhS6K alloy. Strength Mater. 1972;4(2):151–8.

151. 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):20–5.

152. Zeni JA, Higginson JS. Gait parameters and stride-to-stride variability during familiarization to walking on a split-belt treadmill. Clin Biomech. 2010;25(4):383–6.

153. 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):136–44.

154. Harrington ME, Zavatsky AB, Lawson SEM, Yuan Z, Theologis TN. Prediction of the hip joint centre in adults, children, and patients with cerebral palsy based on magnetic resonance imaging. J Biomech. 2007;40(3):595–602.

155. Zeni JA, Higginson JS. Knee osteoarthritis affects the distribution of joint moments during gait. Knee. 2011;18(3):156–9.

156. Winter DA. Biomechanics and Motor Control of Human Movement. Fourth. Waterloo, Ontario: John Wiley & Sons, Inc.; 2009. 1–370 p.

157. Winter DA. Kinematic and kinetic patterns in human gait: Variability and compensating effects. Hum Mov Sci. 1984;3(1–2):51–76.

158. Seeley MK, Park J, King D, Ty Hopkins J. A novel experimental knee-pain model affects perceived pain and movement biomechanics. J Athl Train. 2013;48(3):337–45.

159. Holsgaard-Larsen A, Thorlund JB, Blackmore T, Creaby MW. Changes in total lower limb support moment in middle-aged patients undergoing arthroscopic partial meniscectomy — A longitudinal observational cohort study. Knee. 2019;26(3):595–602.

160. Mandeville D, Osternig LR, Chou LS. The effect of total knee replacement on dynamic support of the body during walking and stair ascent. Clin Biomech. 2007;22(7):787–94.

161. Willy RW, Bigelow MA, Kolesar A, Willson JD, Thomas JS. Knee contact forces and lower extremity support moments during running in young individuals post-partial meniscectomy. Knee Surgery, Sport Traumatol Arthrosc. 2017;25(1):115–22.

162. Kepple TM, Siegel KL, Stanhope SJ. Relative contributions of the lower extremity joint moments to forward progression and support during gait. Gait Posture. 1997;6(1):1–8.

163. Kim YH, Kim HS, Hwang SJ, Myeong SS, Keum YK. Contributions of the lower extremity joint on the support moment in normal walking and, in unexpected step-down walking. Vol. 19, Journal of Mechanical Science and Technology. 2005. p. 371–6.

164. Simonsen EB, Dyhre-Poulsen P, Voigt M, Aagaard P, Fallenlin N. Mechanisms contributing to different joint moments observed during human walking. Scand J Med Sci Sport. 1997;7(1):1–13.

165. Bruijn SM, Van Dieën JH. Control of human gait stability through foot placement. J R Soc Interface. 2018;15(143).

166. Taylor AL, Wilken JM, Deyle GD, Gill NW. Knee extension and stiffness in osteoarthritic and normal knees: A videofluoroscopic analysis of the effect of a single session of manual therapy. J Orthop Sports Phys Ther. 2014;44(4):273–82.

167. Granata KP, Padua DA, Wilson SE. Gender differences in active musculoskeletal stiffness. Part II. Quantification of leg stiffness during functional hopping tasks. J Electromyogr Kinesiol. 2002;12(2):127–35.

168. Visser LC, Stramigioli S, Carloni R. Robust bipedal walking with variable leg stiffness. Proc IEEE RAS EMBS Int Conf Biomed Robot Biomechatronics. 2012;1626–31.

Appendix A – Inter-Subject Variability of Hip, Knee, and Ankle Net Internal Sagittal Plane Moment Waveforms for all Participants

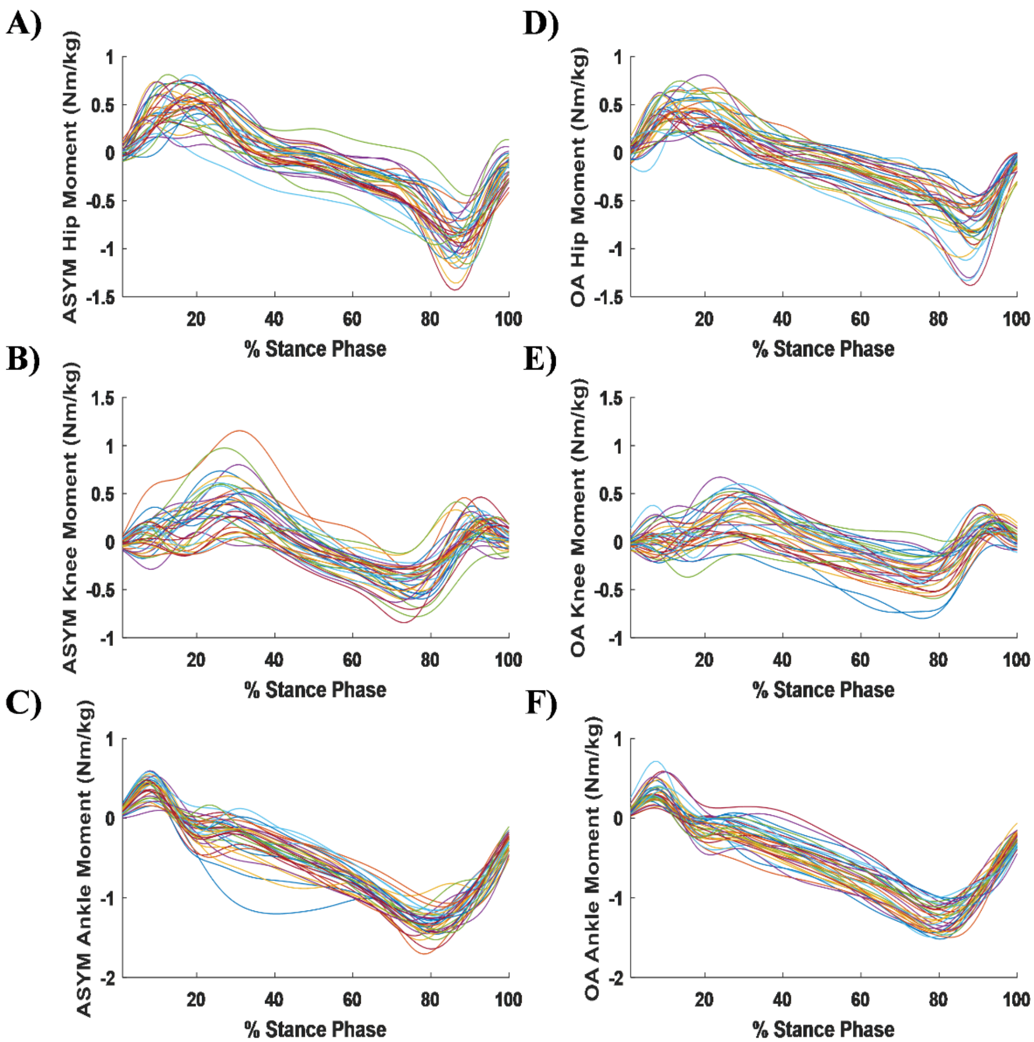

Figure A.1: Net internal sagittal plane moment ensemble averaged waveforms for ASYM individuals for the hip (A), knee (B), and ankle (C), and individuals with knee OA for the hip (D), knee (E), and ankle (F) at T0 time normalized to stance phase and amplitude normalized to body mass. Hip and knee extension moments are positive and flexion moments are negative whereas dorsiflexion moments at the ankle are positive and plantar flexion moments negative.

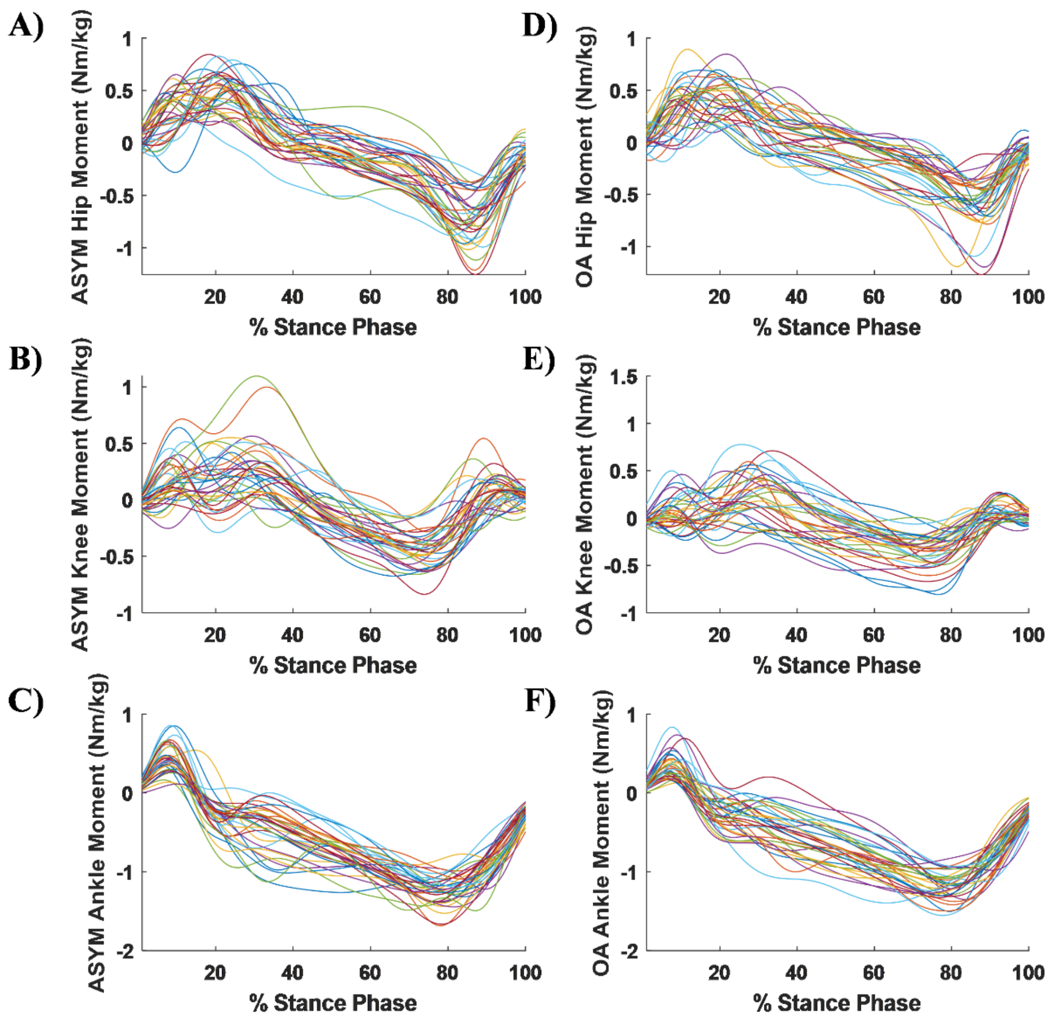

Figure A.2: Net internal sagittal plane moment ensemble averaged waveforms for ASYM individuals for the hip (A), knee (B), and ankle (C), and individuals with knee OA for the hip (D), knee (E), and ankle (F) at T1 time normalized to stance phase and amplitude normalized to body mass. Hip and knee extension moments are positive and flexion moments are negative whereas dorsiflexion moments at the ankle are positive and plantar flexion moments negative.

Appendix B – Component Plots Associated with Leg Stiffness Calculation

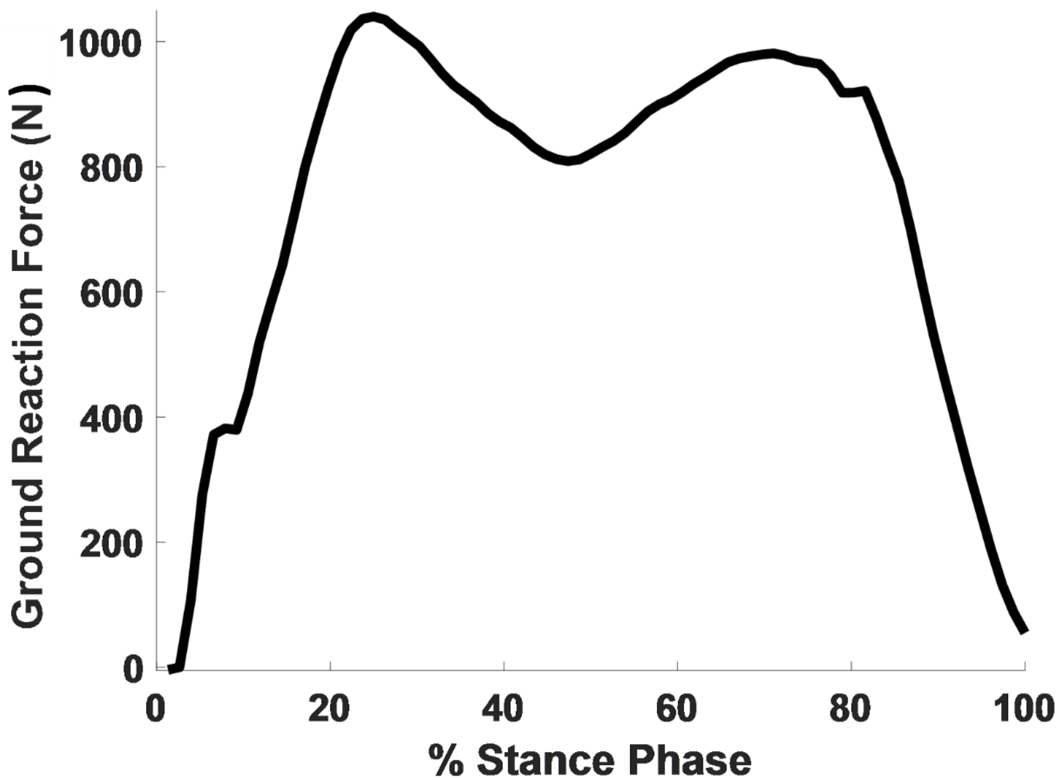

Figure B.1: A sample plot of the ground reaction force vs. percent stance phase.

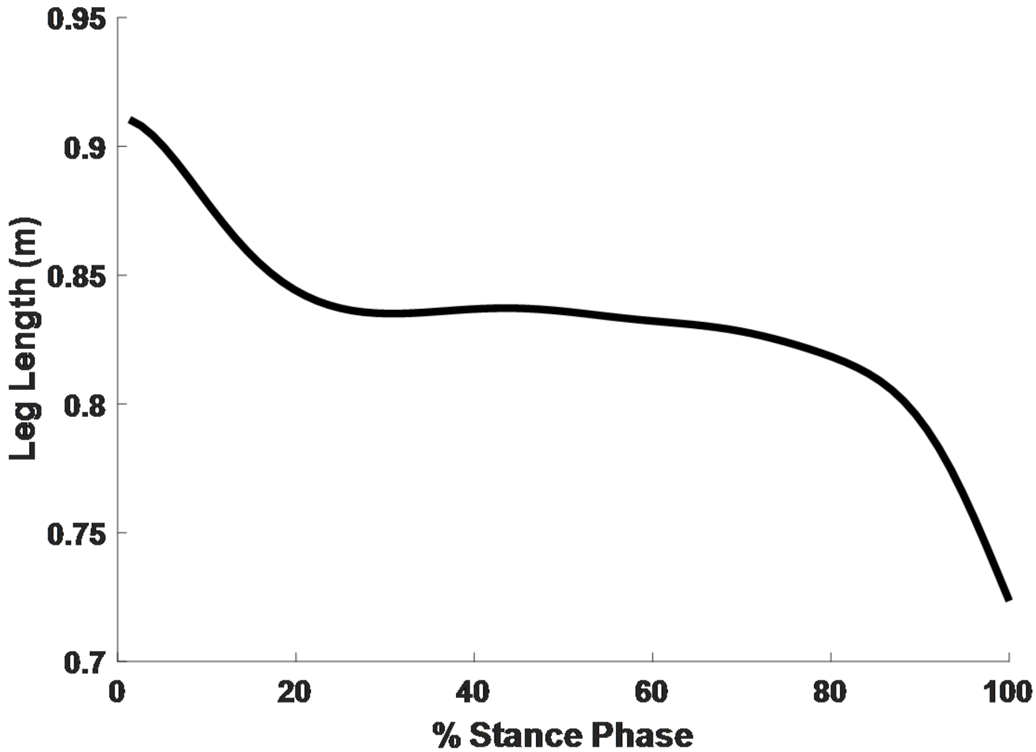

Figure B.2: A sample plot of the calculated leg length vs. percent stance phase.