IMPACT OF PASSIVE RANGE OF MOTION EXERCISES AND STRETCHING IN KNEE OSTEOARTHRITIS PAIN DURING WALKING

A Thesis submitted in partial fulfillment of the
requirements for the degree of
Master of Science

by

DOMINIQUE MARCHELLE OTTONELLO
BFA, Chatham University, 2011

2020
Wright State University

WRIGHT STATE UNIVERSITY
GRADUATE SCHOOL

04/15/2020

I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY Dominique Marchelle Ottonello ENTITLED Impact of Passive Range of Motion Exercises and Stretching in Knee Osteoarthritis Pain During Walking BE ACCEPTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF Master of Science.

_____
Andrew W. Froehle, Ph.D.
Thesis Director

_____
Eric S. Bennett, Ph.D.
Professor and Department Chair,
Department of Neuroscience, Cell Biology and Physiology

Committee on Final Examination:

_____
Andrew W. Froehle, Ph.D.

_____
Kathrin Engisch, Ph.D.

_____
Drew Pringle Ed.D., FACSM

_____
Barry Milligan, Ph.D.
Interim Dean of the Graduate School

ABSTRACT

Ottonello, Dominique Marchelle. M.S. Department of Neuroscience, Cell Biology and Physiology, Wright State University, 2020. Impact of Passive Range of Motion Exercises and Stretching in Knee Osteoarthritis Pain during Walking.

Knee osteoarthritis (KOA), is globally prevalent source of disability for the elderly. This degenerative malady progresses with age and has no cure. It manifests in gait changes and affects overall quality of life. Exercise therapy has been shown to improve knee joint range of motion, stiffness and pain due to KOA. This improvement is due in part to the direct relationship between muscle strength and joint stability. The purpose of this study is to examine how a passive range of motion (ROM) exercises and stretching regimens affect gait-alterations and associated pain from KOA experienced during walking.

Nine KOA subjects were recruited from a local orthopedic clinic and the Fel's longitudinal study, with a final sample size of 7 subjects completing the trial. Subjects performed self-paced walking trials before and after a 4-week long, bi-weekly set of passive ROM and stretching exercises. A trained pre-physical therapy student administered the therapy. Data necessary to assess gait before and after the intervention was acquired via standard gait analysis. Participants rated their pain before the intervention, at the fifth trial and after the intervention ended.

Subjects experienced significant changes in walking speed, stride-length, cadence, peak knee flexion in stance, peak knee flexion in swing and knee flexion/extension (KFE) ROM in swing. Pain did not significantly decrease, remaining largely unchanged. These data supported our hypothesis that a combination of passive ROM and stretching would result in increased ROM and improved patient gait. Our hypothesis that pain would be significantly decreased was not supported. To improve effectiveness of rehabilitation, further research is needed to elucidate the effects of exercise therapy on osteoarthritis-based pain during ambulation.

TABLE OF CONTENTS

LIST OF FIGURES

Figure

LIST OF TABLES

Table

ACKNOWLEDGEMENTS

I am so grateful to have shared in the wisdom, kindness and mentorship of my professors. Your lessons have carried me this far. Thank you to Dr. Froehle for reminding me that walking is a controlled fall; when one limb lags, the other limb rescues it. I would be remiss not to acknowledge Mrs. Kim Hagler for her seeming endless availability and guidance in our program and Erika Gilles for her help. I am indebted to Destinee Biesemeyer and Dr. Susan Edwards for their advocacy.

I reserve my deepest gratitude to my family and my God, whose love encourages me to keep walking, no matter how uncertain the road.

DEDICATION

I dedicate this work to my father, Dr. Domingo Gerardo Ottonello, who often said that knowledge doesn't take up space in the mind, so we have an infinite capacity to learn, to my grandmother, Mrs. Eleanor J. Katic, who called me her "Strong One," but who was the strongest of us all, to my mother Kimberlee and sister Alexis who remain at my side.

Papi, mi alma and Душа моя, I kept my word that I would finish my studies. May you both be in peace, now that you have seen it done.

Here then, immortalized in print until we see each-other again: I love you.

I. INTRODUCTION

Globally, osteoarthritis (OA) affects 303 million individuals (Vos *et al* 2016), and 14 million people nationally (Losina *et al* 2019). OA is a progressive disease compounded by factors such as gait, gravity, load bearing and improper joint-alignment (Sharma *et al* 2001). Of the load-bearing joints, the knee is the most commonly affected (Favre & Jolles, 2016). Knee osteoarthritis (KOA)-related disability is the leading medical condition affecting the elderly. There currently exists no drug to stop osteoarthritis progression (D'Ambrosia 2005), with total knee arthroplasty (TKA) being the intervention of choice for late-stage KOA patients (Beal *et al* 2016). The TKA procedure is costly, making it less accessible to patients. It is also a treatment reserved for late-stage osteoarthritis cases, meaning those that are not yet surgical candidates require other means of pain-relief. Existing pain-relievers such as NSAIDs have the potential to cause gastrointestinal side-effects, and acetaminophen has been shown to not significantly impact osteoarthritis pain (Deyle *et al* 2005). Increasingly, opioids are being prescribed to treat non-cancer pain. They carry a significant risk of addiction and death, however, with one study finding opioid analgesics being the cause of sixty-percent of overdose fatalities, eclipsing overdose deaths caused by any other drug class (Palouzzi *et al* 2011).

Due to a disparity in safe and effective treatment for non-surgical candidates with OA, physical therapy and intervention studies such as ours are needed. Exercised-based physical therapy or exercise therapy, is a system of movements or physical activities that when combined under consistent repetition, encourage patient recovery. It can be tailored to improving specific musculature or broadened to a goal of increased overall physical performance. The aim of exercise therapy is to increase normal range of motion (ROM), performance of daily activities, strengthen muscles, improve balance, and motor function (Hall & Brody, 2005). Studies

involving exercise therapy in treating KOA have shown improved effects on knee ROM, pain, coordination, muscle strength, gait speed and overall functionality (Bennell *et al* 2010; Chamberlain *et al* 1982; Deyle *et al* 2005; Fisher *et al* 1991; Fisher *et al* 1993; Lun *et al* 2015). Where our study differs from past work is that ours has a simplified design executed over a shorter time-span. Simplicity allows the exercise regimen to be applied in a variation of settings which means it will be accessible and more affordable to patients. The shorter duration of our program is beneficial in that patients may be more likely to comply with the therapy and increases accessibility as it is easier to schedule shorter treatments into daily life. These are short-term benefits. It is not known what long-term benefits our study may provide.

In KOA-affected knees, growing biomechanical forces caused by joint malalignment put pressure on lateral, medial and patellofemoral compartments. As such, KOA causes many changes in the biomechanics of walking (Salzman 2010). The combination of these factors results in deconditioning not only at the gait-level but as comorbidities that affect multiple bodily systems (Studenski *et al* 2011). This results in compromised range of motion (ROM) and excess energy expenditure, eventually causing disability (Magee *et al* 2009). Exercise-based rehabilitation has shown promising results in past studies by increasing ROM in KOA patients, with the hope that increased ROM may circumvent the cycle of disability (Baker *et al* 2001; Ettinger *et al* 1997; Fransen, McConnell, & Bell, 2002;). However, more information on how KOA affects gait and what exercises are the most beneficial for KOA subjects needs to be discerned (Walsh *et al* 2009), which makes our rehabilitation-based intervention pertinent.

Our research focused on non-pharmacological, rehabilitation-based interventions. Therapy included passive ROM exercises and active stretching of the muscles around the knee with the hypothesis being that they may aid in pain-management and improve ROM in KOA-

affected subjects. A rehabilitation-based therapy is especially applicable to patients in early stages of OA who do not qualify for surgical intervention, but seek an improvement in mobility and pain-relief. Biomechanical changes in gait such as knee and hip ROM and hip abduction will be examined through gait-analysis as they are important components of gait and commonly altered by KOA and are also related to knee ROM and pain. Given past evidence of improved functionality, pain-relief, and healthy gait-changes observed in KOA patients who have undergone similar combinations of guided stretching and passive ROM, we predict that our exercise therapy program of combined stretching and passive ROM will improve knee ROM and decrease knee-pain levels in ambulatory KOA patients. Background detail will be provided in the following sections including knee anatomy, biomechanics of a normal gait cycle, OA and KOA, and how KOA causes gait pathology.

Knee anatomy

OA affects all components of the knee. To appreciate the pathological changes that take place due to OA in the knee, it is necessary to have a complete picture of healthy knee musculoskeletal and synovial joint anatomy that will be affected by the disease. The knee joint is located at the intersection of the femur and tibia (Perry, 1995). This joint is synovial, meaning its articular surfaces are encapsulated outwardly by fibrous sheaths. The synovial membrane, a serous membrane that lines the inner part of the capsule, produces synovial fluid and surrounds the joint cavity (Moore *et al* 2014). In surrounding the synovial cavity and fluid, the membrane provides a selective environment isolated from other tissues. It also surrounds fat pads, bursae and lines tendons. In synergy with subchondral bone, the synovial membrane nourishes chondrocytes, the cells that produce the founding elements of cartilage. The joint cavity of the

knee houses a potential space. The articulating surfaces of bones are covered with a layer of articular cartilage within the capsule (Moore *et al* 2014).

Articular cartilage functions with two critical mechanical purposes: to provide a smooth floor for load-bearing and to decrease the risk of fracture by distributing stress across load-bearing bones. The major load acting on articular cartilage originates from the contraction of periarticular muscles as they stabilize the joint. In a loading state, cartilage deforms to produce a hydrostatic, self-pressurized lubrication necessary for motion (Brandt, 2001).

The knee is subcategorized as a bicondylar joint, meaning that it moves unidirectionally, but allows for minimal rotation (Komdeur *et al* 2002). There are three interactions between the femur, the tibia and the patella. Two corresponding femorotibial articulations are formed proximally by the lateral and medial femoral condyles, and distally by the lateral and medial tibial condyles (Moore *et al* 2014). The plateau-like surfaces of the tibia that articulate with the femoral condyles are what make up the lateral and medial compartments of the knee (Neumann, 2010). In KOA, the medial compartment is also the most commonly affected compartment (Jones *et al* 2013), hence it was the focus of this study. The area between the tibial condyles, known as the intercondylar space, is divided anteriorly and posteriorly by the presence of two bony eminences, the intercondylar tubercles (Moore *et al* 2014).

The anterior and posterior regions of the intercondylar space houses ligaments that prevent knee hyperflexion or hyperextension (Moore *et al* 2014). The intercondylar space forms a valley, with a lateral facet which is steeper than its medial facet. The lateral facet extends proximally and anteriorly and its slope allows it to stabilize the patella during knee motion (Neumann, 2010). Each femoral condyle has bony prominences called epicondyles that serve as ligamentous attachment sites. The third articulation lies between the femur and the patella.

(Moore *et al* 2014). The patellofemoral joint moves in a gliding fashion. The posterior face of the patella articulates with the femur's medial and lateral surfaces from full extension to 140 degrees of flexion. The patella lowers into the intercondylar space at full flexion (Hehne, 1990).

Epiphyseal trabecular bone absorbs loading in the knee and acts as another shock-absorber in addition to cartilage, which is approximately 1-2 mm thick. After cartilage has deformed to its maximum potential during loading, the corresponding bone beneath it will deform to optimize the contact of opposing joint surfaces which reduces stress. Under high loads, the bone's absorption of force and stress-minimization is crucial compared to that of cartilage. The softness and high elasticity of subchondral bone allows it to absorb energy during loading which protects the cartilage above (Brandt, 2001). While the osteology of the knee can provide stabilization to the joint, it is the soft-tissues such as ligaments and muscles are the primary providers of structure to the joint (Neumann, 2010).

Connective tissue in the form of ligaments and menisci act to stabilize the knee. The major stability of the knee joint in anterior and posterior translation, varus (knee adduction) and valgus (knee abduction) angulation and external and internal rotation of the knee is derived from ligaments (Nordin & Frankel, 2001). Classification of ligaments is divided into extra and intracapsular. Extracapsular ligaments are the lateral and medial collateral ligaments, and the oblique and arcuate popliteal ligaments (Moore *et al* 2014).

The lateral collateral ligament reaches from the femoral lateral epicondyle to the fibular head's lateral surface. It opposes varus, extension and excess external rotation of the knee. The medial collateral ligament originates at the femoral medial epicondyle and inserts on the medial surface of the tibia. It counteracts valgus, extension, and excess internal rotation. Excess knee motion in the frontal plane is regulated by both collateral ligaments (Neumann, 2010). The

oblique popliteal ligament extends posterior to the medial tibial condyle and crosses the posterior intercondylar space toward the lateral femoral condyle where it meshes with the joint capsule (Moore *et al* 2014).

The intracapsular ligaments include the anterior and posterior cruciate ligaments. The anterior cruciate ligament (ACL), extends from the tibia's posterior intercondylar surface to the posteromedial part of the femoral lateral condyle (Moore *et al* 2014). The ACL limits the knee's hyper-extension either by the resisting the femur's posterior translation across the tibia, or the tibia's anterior translation beneath the femur. It does this by progressively tensing during extension, peaking during full knee extension (Neumann, 2010). The ACL also opposes excessive varus, valgus and axial rotation (Neumann, 2010). The posterior cruciate ligament (PCL), reaches from the tibia's posterior intercondylar region to the anterior part of the medial femoral condyle (Moore *et al* 2014). The primary limiter of posterior tibial translation is the PCL. Varus, valgus and axial rotation are also resisted by the PCL, but unlike the ACL, it opposes knee flexion (Neumann, 2010).

The lateral and medial menisci are half-moon-shaped fibrocartilaginous plates on the tibia's articular surfaces. They attach at the tibia's intercondylar region and blend externally at the knee-joint capsule. These provide stability during motion, proprioception, decrease compressive stress (Neumann, 2010), and exhibit migratory movement against the tibial plateau as contact-points between the femur and the tibia vary during motion (Moore *et al* 2014).

Muscles actively stabilize the knee by doing negative work. Upon joint-movement, for example, if the quadriceps contract to extend the knee, a partially stretched muscle or muscle group can become greatly stretched which can allow it to absorb a lot of energy (Brandt, 2001). The anterior compartment of the thigh contains the primary knee extensors, which are the

quadriceps femoris group. This is comprised by rectus femoris, vastus lateralis, intermedius and lateralis. Rectus femoris originates at the anterior superior iliac spine, vastus lateralis does so at the femur's greater trochanter and lateral linea aspera, vastus intermedius has a proximal attachment at the anterolateral femoral shaft, and vastus medialis originates at the femur's intertrochanteric line and medial edge of the linea aspera. All muscles of quadriceps femoris unite to form the quadriceps tendon, and indirectly share a common insertion point on the tibial tuberosity by way of the patellar ligament. Fibers of the quadriceps tendon envelope the patella (Moore *et al* 2014).

The posterior compartment of the thigh involves the hamstring group which flex the knee. These include semimembranosus, semitendinosus and biceps femoris. Each muscle shares a common origin at the ischial tuberosity, except the long head of biceps femoris, which originates at the femur's linea aspera and lateral supracondylar line. Semimembranosus inserts on the posterior region of the tibial medial condyle. Semitendinosus distally attaches to the medial surface of the superior tibia and biceps femoris inserts in the lateral head of the fibula. Secondary muscles that aid in knee-flexion include sartorius, gracilis and gastrocnemius (Moore *et al* 2014).

Sartorius, located in the anterior thigh, synergistically acts to flex the knee. It originates at the anterior superior iliac spine and inserts on the superior part of the medial tibia. Gracilis is a member of the adductor compartment. It minorly flexes and rotates the flexed knee. Originating at the pubic body and inferior ramus, gracilis distally attaches to the superior region of the medial tibia (Moore *et al* 2014).

Biomechanics of a normal gait cycle

To comprehend the pathology of a KOA-affected gait, one must understand the composition of a normal gait cycle. A cycle lasts from the time a heel touches the ground, known as heel-strike, to the consecutive heel-strike of the same foot. The amount of distance covered in one gait cycle is known as a stride (Delisa *et al.*, 2007). The duration of a gait-cycle is known as the cycle time. Stance-phase and swing-phase are the two subdivisions of a cycle (Umberger 2010).

Stance phase, when a leg is loading or weight-bearing, represents 60 percent of the cycle (Umberger 2010). Depending on the moment in stance, an individual may be in double or single-limb support. Per cycle, there are two periods of double limb support and two of single limb support. During double-limb support, both feet are on the ground as the body begins to shift its weight to take a forward step. The forward foot has just landed in heel-strike. The other foot in preparation to be airborne, has its heel raised so that only the toes contact the ground in a stage called toe-off (Whittle, 2008). It is in double-limb support that weight is transferred from lagging to leading leg, so that the leading leg assumes the responsibility of load-bearing. Weight is released from lagging leg that started the transfer, so that it may leave the ground in a forward step. During this period from midstance to terminal stance, the knee requires a stabilizer under loading. The quadriceps resist knee flexion collapse beneath weight during single limb support (Nordin & Frankel, 2001). In addition to the quadriceps, hip abductors, erector spinae, gluteus maximus, anterior tibialis and the hamstrings act to brace the supporting (leading) leg and trunk. Muscles balance deceleration and acceleration to defy gravity, which produces ground-clearance and forward motion (Delisa, 1998).

Deceleration occurs in stance by concurrent interactions of the hip, knee and ankle (Delisa, 1998). The hip is flexed at 40 degrees when heel-strike occurs, and the ankle is dorsiflexed. For the foot to completely contact the ground in the foot-flat stage, anterior tibialis and smaller dorsiflexors must undergo quick eccentric contractions. The quadriceps will also eccentrically contract at the same time to minimize knee flexion. The trunk is at its lowest point at this moment of the cycle. The hip extends toward the pelvis, which gives the trunk forward momentum. Extensors that act on the hip such as gluteus maximus and the hamstring group, regulate the trunk's forward momentum. Toe off occurs to prime the foot to be lifted from its contact point. Stance phase ends in single-limb support (Delisa *et al* 2007).

The other 40 percent of the gait cycle is non-weight-bearing. Complimentary to the deceleration of a leg in stance phase, the opposite leg is in the process of releasing weight or commencing swing phase. It is divided into three stages, acceleration, mid-swing and deceleration. Forward motion of the swing limb is characteristic of the acceleration period and the leading foot exhibits clearance, that is, it does not touch the ground. Plantar flexion of the ankle results due to concentric contractions of posterior tibialis, soleus, gastrocnemius and plantar flexors such as flexor hallucis longus, flexor digitorum longus and fibularis longus and brevis (Malanga & Delisa, 1998). The hip and knee are also flexed, with knee flexion being influential to toe clearance. The knee reaches its peak flexion during the beginning of swing phase (Whittle, 2008). For a successful clearance, the knee must be flexed to 60 degrees (Piazza & Delp, 1996). Towards the end of the phase, the leg in swing decelerates through contraction of the hamstrings to begin the gait-cycle anew with another heel strike (Delisa *et al* 2007).

Other variables relevant to this study are step-length, stride-length, cadence, speed and moments. Step-length is the distance one foot moves forward in front of the other during swing

phase. A stride-length consists of two step-lengths by the same foot. The number of steps taken per minute is the cadence. Walking speed is the distance the body travels per time. Speed directly correlates with two step-lengths, which are based on the duration of swing-phase. If the foot doesn't clear the ground, swing-phase is halted, resulting in a limited step-length that slows walking speed (Whittle, 2008).

Osteoarthritis

Clinical presentation and classifications

Altman et al 1986 defined osteoarthritis (OA) as an amalgam of conditions that result in joint signs and symptoms indicative of damaged articular cartilage and alterations in joint-margins and subsequent bone culminating in pain and disability. Research of progressed OA suggests that the already constrained ability for cartilage to self-heal fails due to structure-mechanical factors, and the work of degradative enzymes that exacerbate cartilaginous disintegration, (Myers, 2004) fibrillation—the formation of vertical clefts and loss of surface integrity in cartilage (Brandt, 2001) and ulceration that is irreparable (Myers, 2004).

The disease presents with clinical signs such as a principle symptom of joint pain, inflammation and deformity, stiffness of varying severity and muscle weakness. Joint inflammation signs involve local erythema, heat, swelling, and diffuse tenderness to palpation (Brandt, 2001). OA can be classified clinically, pathologically or radiographically. The reference standard has been radiographic (Zhang & Jordan, 2008), with the Kellgren Lawrence scale (KL) remaining the accepted model for osteoarthritic radiographic diagnosis and severity grading (Braun & Gold, 2012; Kohn *et al* 2016). The scale consists of 5 radiographic levels: KL grade 0, "absent," in which there are no radiographic features of OA present, KL grade 1, "doubtful,"

during which a radiograph shows doubtful joint space narrowing with possible osteophyte formation, grade 2, “minimal,” a radiograph that shows possible narrowing of the joint space with definite osteophyte formation, grade 3, “moderate,” where a radiograph demonstrates definite joint space narrowing, moderate osteophyte formation, some sclerosis, and possible deformity of boney ends, and grade 4, “severe,” where severe narrowing of the joint space can be appreciated, large osteophytic formation, marked sclerosis and gross deformity of boney ends (Brandt, 2001; Kohn *et al* 2016).

There are two subdivisions of OA, primary and secondary OA. Subjects from our study have primary OA. Primary OA is idiopathic, the etiology of which remains unclear, but is tied to genetic factors, ethnicity, biomechanical wear, and age-based physiological changes (Johnson & Hunter, 2014). Clinicians recognize three subsets of primary OA presentation: generalized OA, primary generalized or nodal OA, and erosive OA (Myers, 2004).

Epidemiology and Risk factors

More than 80% of individuals over 55 years old bear radiographic hallmarks of OA. Of that grouping, some will be asymptomatic, with 10-20 percent who present with some level of disability (Brandt, 2001). Prevalence estimates are conflicting due to inconsistent diagnoses however, several recent epidemiologic studies have provided a window of the frequency of this disease. The Framingham study found the prevalence of radiographic KOA in adults >45 years of age to be 19.2%, while the Johnston County Osteoarthritis Project yielded a prevalence of 27.8% of participants. Of subjects >60 years old, the Third National Health and Nutrition

Examination Survey (NHANES) found 37% had KOA (Zhang & Jordan, 2008). What is known is that at every joint, OA prevalence rises with age. The strongest risk factor for OA is age.

Gender is a major risk factor for OA and bears correlations with age and race. Women are twice as likely to be affected by OA than men, according to Brandt, 2001. The Fifth Korean National Health and Nutrition Examination Survey, which involved 9,512 subjects ≥50 years of age, with radiographic KOA defined as KL grade ≥2, found men to have a radiographic KOA prevalence of 21.1% (95% CI: 19.6–22.8%), compared to 43.8% in women. Women >75 years of age are also 30% more likely to have KOA compared to men in the same age range (Brandt, 2001).

Obesity is a known risk factor for OA, and particularly KOA. The correlation between disease progression and weight was demonstrated by a study that found that women who lost 5 kg, decreased their risk of new symptomatic KOA development by 50%. Decreased weight-loss in the same study, also corresponded with decreased risk of radiographic KOA (Felson *et al* 2000).

Pathology and Pathogenesis

It is inaccurate to describe OA as a degenerative disease or progressive wear and tear, though it bears degenerative features. An encompassing depiction of OA is as a disease of the entire joint, meaning, periarticular musculature, neuromuscular apparatus, synovium, articular cartilage, ligaments and subchondral bone with pathologies in each that contribute to pathomechanics that result in disability. If one views the synovial joint as an organ, OA is organ failure on multiple levels (Brandt, 2001).

Though the etiology of OA is thought to be multifactorial, the primary changes of OA commence in cartilage (Brandt, 2005). Current findings suggest that the synovial membrane is not passive in OA development, but when inflamed, produces a host of proinflammatory mediators that contribute to cartilage break-down (Sellam & Berenbaum, 2010). These mediators are crucial to the development and progression of OA as they influence signal transduction pathways and pathologically alter cell-behavior (Wojdasiewicz *et al* 2014).

Synovitis is the inflammation of the synovial membrane seen on ultrasound as membrane thickening and / or joint effusion (Pisetsky & McCleane, 2009). Researchers examined a sample of 535 patients for a link between KOA-associated knee pain and synovial thickening using MRI with contrast. They found that in afflicted knees of moderate pain levels, 80% of patients had synovitis (Baker *et al* 2010).

To date, OA is not classified as an inflammatory disease due to a presentation with mild leukocytosis (<2,000 WBC/microliter) upon synovial fluid examination (Brandt, 2005). However, research suggests a strong relationship between inflammatory pathways and altered cartilagenous synthesis and catabolism. Ayral and colleagues extrapolated that medial synovitis could be predictive of escalated medial cartilage breakdown in KOA. OA affected cartilage exhibits highly metabolically active chondrocytes that may contribute to a phase of cartilaginous thickening and homeostasis known as Compensated OA. This stage may provide functionality for decades, but the cartilage produced in this stasis lacks the structural integrity needed to withstand repetitive mechanical forces and will ultimately give under pressure without regenerating. What causes the structural aberrations in cartilage is believed to also contribute to a decreased synthesis of proteoglycans. The sudden lack of proteoglycan production results in a

full-thickness loss of cartilage, or bone on bone, which is a hallmark of end-stage OA (Brandt, 2005).

KOA manifests with periarticular muscle dysfunction in the form of weakness, as well as decreased strength in other muscle groups of the lower limb (Tan *et al* 1995), (Hinman *et al* 2010). The source of muscle weakness from OA is not fully understood. It is thought that muscle disuse atrophy occurs secondary to pain, where KOA indirectly induces atrophy (Slemenda *et al* 1997), but research suggests that inability to activate muscles voluntarily, arthrogenic muscular inhibition (AMI), may be a direct effect of KOA (Liikavainio *et al* 2006), (Young, 1993).

How KOA causes gait pathology

Pain due to joint degeneration is one cause of gait pathology due to disability and from the compensatory measures it causes (Myers, 2004). Patients with joint pain develop an antalgic gait with a limited ROM, slowed stride speed, short steps, and may limp or be unable to bear weight. Even in the instance that weight-bearing is tolerated by the patient, joint buckling due to pain can alter gait (Salzman, 2010). Patients with KOA have increased stride frequency per distance travelled (Mills *et al* 2013), and deviations in stance-phase knee-flexion (Mandeville *et al* 2009). Other gait changes in KOA patients include a smaller stride and longer lasting stance than healthy samples (Baliunas *et al* 2002); (Kubota *et al* 2007); (Teixeira & Olney, 1996).

The importance of gait speed in geriatric assessment, adaptation of rehabilitation goals and life-span estimation has garnered it the label, "the 6th vital sign" (Studenski *et al* 2011). Life-expectancy and gait speed are linked, with faster gait being indicative of a longer life-span (Studenski *et al* 2011). KOA patients are known to have a diminished gait speed, with speed

having a relationship inverse to disease severity (Astephen *et al* 2008). For KOA subjects, slower walking has been implicated to be an accommodation to reduce medial compartment loading and its accompanying pain (Robon *et al* 2000). That pain significantly correlates with increased KL scores (Sanghi *et al* 2011), also supports compensation as a reason for decreased gait speed in KOA patients.

Mündermann *et al* 2004 found that KOA patients with a KL grade ≤2 exhibited decreased maximum knee adduction moments compared to asymptomatic controls or severe KOA KL grade ≥3 patients of similar age and sex distributions. A KOA subject's slow gait may be the product of compensation through a need to reduce adduction moments during walking, to accommodate for painful load-bearing. Low adduction moments may result in slower disease progression (Miyazaki *et al* 2002).

KOA modifies gait by causing changes in moments and ROM during dynamic motion (Perry, 1995). In KOA, knee ROM deviates during dynamic movements (Perry, 1995). Kaufman et al. 2001, found significant compensatory reductions of internal knee extensor moments in KOA subjects. Female subjects had significantly larger knee extensor moments and greater knee flexion. Non-KOA subjects did not exhibit these osteokinematic changes in ROM.

Joint alignment is another component of gait altered by KOA involvement. In stance, medial compartment-based KOA causes the knee to lean medially and displaces the foot, which results in increased load on the medial tibial plateau (Perry, 1995). Increased load on the medial side of the tibia corresponds with a decrease in medial compartment space (Gudbergsen *et al* 2013). To accommodate for the deviated foot, the hip abducts, which moves the trunk laterally. Eventually, the knee adducts in excess, into varus (Perry, 1995). An alignment more than 5-degrees valgus or varus is associated with greater loss of function (Sharma *et al* 2001). In stance,

varus becomes more pronounced and in swing phase it is less severe (Chang *et al* 2004). Varus and valgus deviations are known factors contributing to compressive load, with varus affecting particularly the medial compartment (Sharma *et al* 2001).

Muscle fatigue causes changes in proprioception at the level of the joint, compounding balance impairments and increasing chance of injury (Miller & Bird, 1976). A statistically significant correlation between muscle fatigue and pain was shown in KOA patients, with subjects that had higher pain scores having lower voluntary quadriceps strength (Orielly *et al* 1998). Given that KOA causes gait changes in balance, energy metabolism and joint somatosensation, successful KOA intervention therapy must include strengthening of affected muscle groups (Minor, 1994).

Therapy

Because there is no cure for OA, comprehension of available therapeutics is necessary. Treatments span a range from mild to invasive, including patient education and psychologic support via regular phone-calls from nursing staff, to exercise and stretching regimens, a cane or other means of ambulatory support, resting-splints, non-narcotics, analgesics, anti-inflammatory agents, intra-articular corticosteroid injections, biologics, joint-aspiration for pressure relief and in severe cases, joint arthroplasty (Myers, 2016; Mathiessen & Conaghan, 2017).

Clinicians aim to control OA symptoms, the cardinal symptom being pain, through pharmacological intervention. The depth of medicinal and invasive treatments applicable to OA symptom-management is beyond the scope of this paper. Occasionally, exercise therapy is prescribed to help manage pain from OA (Brandt, 2001), (Hunter *et al* 2008). Our research

involving stretching and passive ROM falls into the category of non-medicinal or exercise therapy for KOA.

There are many randomized controlled trials that lend support to exercise being a beneficial therapy for KOA, with results ranging from increases in muscle strength, to pain diminishment, increased ROM, balance and decreased disability (Bennell *et al* 2010; Chamberlain *et al* 1982; Deyle *et al* 2005; Fisher *et al* 1991; Fisher *et al* 1993; Lun *et al* 2015; Minor, 1994; Penninx *et al* 2001; Røgind *et al* 1998). Minor, 1994 recommends that the outcomes of an exercise program targeted to an OA patient should include impairment reduction such as a decrease in joint-pain and improved joint ROM and strength, as well as enhanced functionality in the form of gait normalization and normal activities. Any prescribed exercise program should protect the affected joint from further breakdown through attenuation of joint forces, limited joint stress and corrected biomechanics. Therapy should be structured so that the general conditioning can be maintained by patients throughout daily life as a protection against secondary illness and worsening KOA progression due to sedentary life-style. A common finding in KOA patients is that the disease affects motion in all joints of the lower limb, so that the hip, knee and ankle experience a decrease in ROM. Because of this, an exercise approach that addresses ROM, such as the protocol our study was based on, is often indicated for individuals with KOA.

Evidence exists that exercise may improve KOA patient inflammatory cytokine levels. Zhang *et al* 2013 performed a 4-week intervention with a frequency of 4 days a week, twice-daily. The post-therapy synovial fluid analysis yielded significantly lower TNFα and CRP levels in both groups compared to baseline results, suggesting that lower inflammatory mediator levels were not simply due to the administration of diclofenac. The therapy group had significantly

lower TNFα and CRP values compared to those of the control group, indicating that exercise may have a positive therapeutic effect on inflammation mediation.

Exercise has other benefits for KOA patient health. Penninx et al 2001 provided data that support that aerobic or resistance exercise can protect functionality and decrease pain during activities of daily living in elderly populations. Daily life activities were defined as independent bed to chair transfers, eating, dressing, using the toilet, or bathing. Patients were ≥60 years of age with radiographic KOA, KL-grade unspecified, who reported knee pain most days of the month and did not exercise more than once a week for greater than twenty minutes. Participants from either program had a 0.57 times decreased risk of developing disability and had a significantly higher probability of remaining disability-free for 18 months compared to controls. In separate analyses on disability incidence in individual items of daily activity, exercise was a significant protection against acquiring disability in 4 out of 5 of the defined activities. Both exercise groups also reported decreased knee pain. In other studies, exercise has shown to not only to maintain, but increase functionality.

Common areas of improved functionality among KOA patients who participate in exercise programs are in muscle strengthening, enhanced endurance, increased gait-speed and pain diminishment (Jansen *et al* 2011). An intervention done by Røgind *et al* 1998, showed functional improvement in KOA-based pain and gait-speed. Bilateral KOA patients who had a KL grade of 2-3 underwent biweekly training for 3 months. The intervention consisted of mobility training, venous therapy, lower extremity and truncal muscle strengthening, and flexibility and coordination conditioning. Therapy included physical therapist-guided repetitive exercises for quadriceps, hip adductors, hip abductors, hamstrings, gluteus maximus muscles, erector spinae muscles, and abdominal muscles. Flexibility was addressed through stretching of

the calf muscles, quadriceps, hamstrings, gluteus maximus, lower back muscles and pectoralis major, with a focus on hip adductors. The combination of exercise and stretching improved isokinetic and isometric muscle strength, with a 20% increase in quadriceps strength. The intervention also increased walking speed by 13%, decreased overall pain, weight-bearing pain, and pain at rest scores, and decreased crepitus frequency on the least effected side (Røgind *et al* 1998).

Exercise has benefits in addition to improved functional capacity in KOA patients. Research consistently shows that physical fitness training also can reduce KOA-associated knee pain (Baker *et al* 2001; Bautch *et al* 1997; Ettinger *et al* 1997*;* Fransen *et al* 2001; Hopman-rock &Westhoff, 2000; Kovar *et al* 1992; O'Reilly *et al* 1999; Penninx *et al* 2001; Petrella & Bartha, 2000; Quilty *et al* 2003; Røgind *et al* 1998; Schilke *et al* 1996; van Baar *et al* 1998). A study comparing two groups of KOA subjects who underwent a hip or knee muscle strengthening regimen showed decreased WOMAC and KOOS pain scores of statistic and clinical significance after finishing their exercise therapy (Lun *et al* 2015). A trial that examined the correlation between hip abduction strengthening exercises and pain, implemented six side-lying and standing standardized exercises to strengthen hip abductors and adductors in three sets of 10 repetitions, supplemented with ankle weights or therapy-bands. With increased hip abduction strength, pain and functionality were significantly improved. Eighty percent of the strengthening group had more functionality during walking and less pain compared to sixteen percent of the control group (Bennell *et al* 2010). Though exercise alone increases functionality, exercise combined with passive ROM manipulation appears to best benefit patient pain levels (Jansen *et al* 2011).

A review of 12 trials compared the results of strength training alone, exercise therapy alone (meaning a combination of aerobics, strength training and active ROM), and exercise with passive ROM to non-active controls and found the greatest sized effect for pain-relief was through programs that combined exercise with passive ROM. Trials that used this combination yielded an effect size of 0.69 (95% CI 0.42 to 0.96) on pain, compared to exercise alone which had an effect size of 0.49 (95% CI 0.19 to 0.49) and strength training that gave an effect size of 0.38 (95% CI 0.23 to 0.54) (Jansen, 2011). A combination approach is further supported by results from the Osteoarthritis Research Society International (OARSI). OARSI reviewed a series of expert guidelines based on evidence and found that 21/21 published guidelines recommended that KOA patients maintain a combined exercise program of aerobic walking, quadriceps strengthening and passive ROM, with pooled effect sizes for pain relief in the moderate range (Zhang *et al* 2008).

In further support for combined modalities, Falconer *et al* 1992 ran a study that compared a control group who received sham ultrasound treatments and exercise therapy with a group of KOA patients treated with ultrasound and underwent exercise intervention. Patient inclusion criteria was a KOA diagnosis with the presence of knee pain, crepitus, a limitation of at least 10˚passive flexion and extension, boney enlargement and chronic knee motion limitation for at least 6 months. Radiography in most cases documented joint-space narrowing and osteophyte presence, indicative of moderate levels of KOA for the majority. TKA subjects were included provided they were 6-months post-operation. Exercise was performed in a physical therapy clinic and consisted of 30 minutes of passive stretching, broken into 5-15-minute bouts of stretching and cool-down periods, along with anterior-posterior and posterior-anterior grade 3 and 4 manual mobilization tibiofemoral glides. Passive ROM exercises of knee flexion and extension, and

isometric strengthening followed glides. Other full ROM performed included quad sets, knee to chest, straight-leg raises and bridging. Exercises were done in repetitions of 10, with 5-second holds per repetition and 5-second rests between. The frequency of the intervention was 12 treatments, 2-3 times per week, for a duration of 4-6 weeks. Seventy seven percent of subjects increased their active knee ROM, 71% had decreased knee pain and 72% showed a rise in gait velocity. Ultrasound was found to have no impact on mobility enhancement, which bolstered support for stretching and ROM as effective treatment for increasing functionality in KOA patients.

Our intervention protocol was based off work by Deyle *et al* 2005. They compared the effects of passive ROM, active ROM, stretching and strengthening exercises on a clinic treatment group of KOA patients and a home treatment group of KOA patients. The results of their study support a combination of ROM and stretching as a beneficial treatment for KOA pain, stiffness and overall functionality. Subjects had varying levels of disease with 3% KL=0, 24% KL=1, 41% KL=2, 19% KL=3 and 12% KL=4.

Participants in the clinic group attended 8 sessions at the physical therapy clinic where they received passive joint mobilization in addition to, and sometimes during their passive ROM exercises (Deyle *et al* 2005). Passive joint mobilization was performed in the Maitland mobilization technique, a treatment that is based on oscillation intensity (Moon *et al* 2015). Passive ROM included knee extension alone, knee extension with varus and knee extension with valgus, and knee flexion alone and knee flexion with internal rotation. Manual stretching of quadriceps femoris, the hamstrings, gastrocnemius, knee adductors, iliopsoas, tensor fasciae latae and the iliotibial band were completed to muscle end-length. They also performed a series of strengthening exercises and active ROM. Strengthening exercises included daily statis quad sets

in knee extension, standing terminal knee extension performed 3 times a week, closed chain progression from least to most difficult performed 3 times a week, seated leg presses weight-lessened partial squats, and step ups. Stretching exercises included the standing calf stretch, supine hamstring stretch, and prone quadriceps femoris stretch. Active ROM exercises involved positioning the knee in mid-flexion to full-extension and placing the knee in mid-flexion to full-flexion. Subjects were advised to continue riding a stationary bike if it was part of their routine prior to the study. The clinic group's exercise supervision consisted of 1 exercise instruction lesson and 7 supervised exercise appointments (Deyle *et al* 2005).

The home exercise group did not receive passive ROM or Maitland mobilization. They completed the same series of stretches, strengthening exercises, and active ROM exercises and were also encouraged to maintain riding a stationary bike if it was part of their own exercise routine prior to participation in the study. Two instruction sessions were provided for them and they had no exercise supervision (Deyle *et al* 2005).

Both groups exhibited 6-minute-walk test distance improvements averaging 10% at 4-weeks, without major changes between 4-8 weeks. In comparison, though both groups had improved baseline and 4-week-mark average WOMAC scores, the clinic treatment benefited twice the amount that the home exercise group did. The clinic group's average WOMAC score improved by 52% compared to the home exercise group who yielded an average improvement of 26 percent. Between 4-8 weeks, neither group experienced a significant change in WOMAC scores. Both 6-minute walk test distances and WOMAC scores remained significantly improved at the 1-year follow-up for both groups. The clinic group's average 1-year WOMAC scores were 32% improved versus a 28% improvement in the WOMAC scores of the home exercise group. Also at the 1-year-mark, patients were queried about whether they were medicating their KOA.

Forty-eight percent of the participants from the clinic group were taking medicine for their KOA compared to 68% of the home exercise group. Questionnaire results showed that the clinic group was more satisfied with overall results of the intervention (Deyle *et al* 2005).

A key difference between the therapies trialed by both groups is that the home exercise program did not include passive ROM, passive manual stretching or Maitland mobilization. That both groups positively responded to either exercise therapy program in improved WOMAC values and walking trials, strengthens the existing trend that exercise is beneficial to KOA pain, stiffness and functionality. The study also provided data that suggest that at least a year-long lasting improvement in symptoms may be another benefit of exercise therapy. That the clinic group's WOMAC values and 6-minute walking trial distance measurements showed greater improvement compared to those from the home exercise group, supports the argument that an intervention involving supervised passive ROM, stretching and mobilization is more efficient than a home exercise program of 8-weeks duration.

II. MATERIALS AND METHODS

Subjects

Nine subjects were recruited from the Fels Longitudinal Study (Sherwood & Duran, 2014) and a nearby orthopedic surgery clinic. All reviewed experimental protocol prior to consent and provided informed consent prior to participation. Prior to signing consent forms, two subjects declined to participate in the study, leaving 7 subjects who completed the intervention. Subjects were included if they were diagnosed with unilateral radiographic KOA, staged mid/early with a KL grade of 2-3, ≥45 years of age and ineligible for TKA intervention. Exclusion criteria included: diagnosis of OA in the spine, hip, foot or ankle, previous lower extremity joint surgical replacement or intervention less than 6 months prior to testing, skeletal or soft-tissue damage to the trunk, pelvis, spine or lower extremity, inserts, orthotics or gait-associated diseases. The Wright State University Institutional Review Board approved this study prior to subject recruitment or data collection.

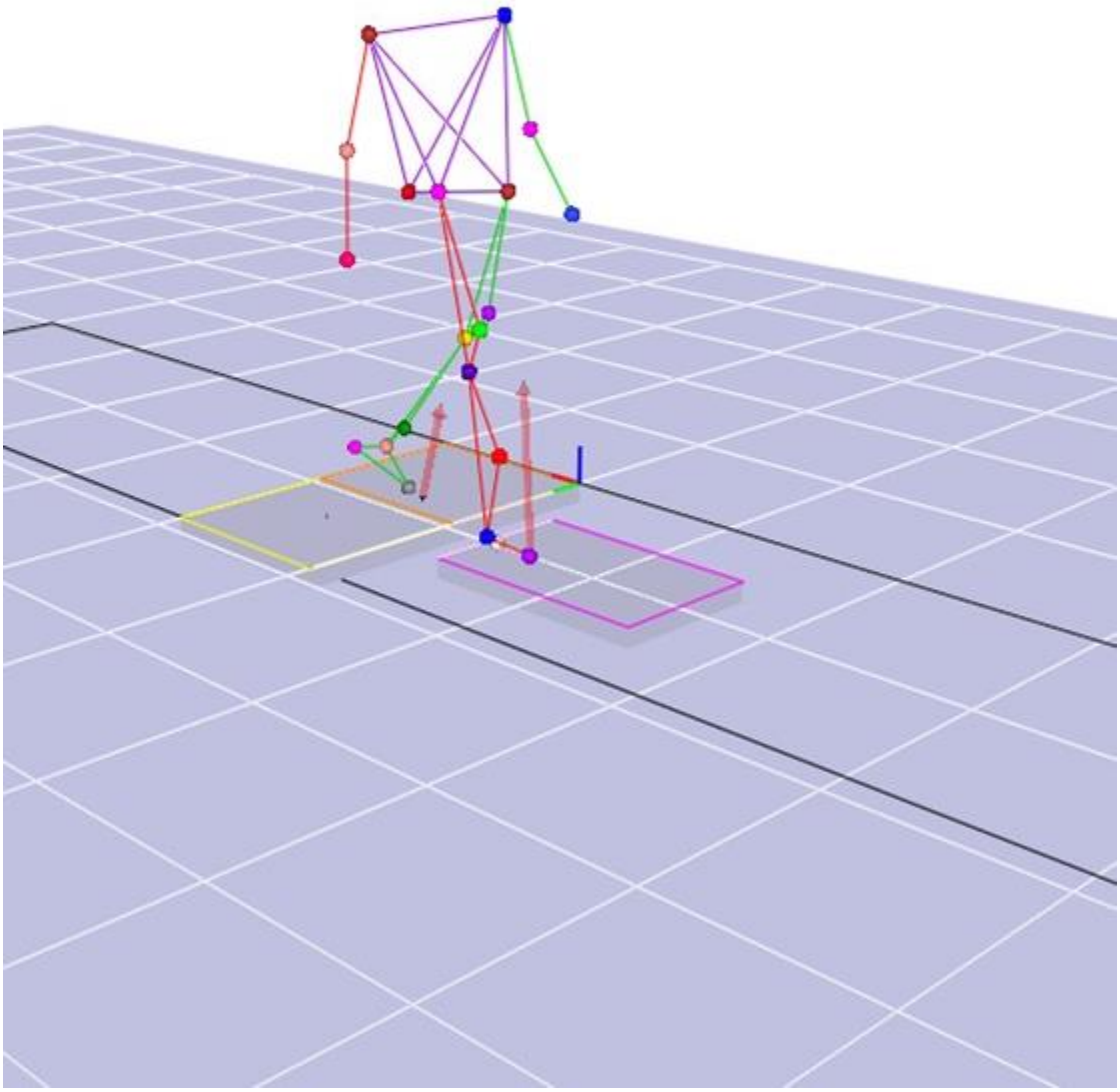
Data collection and Instrumentation

Per Lohmann *et al* 1988, anthropometric data were gathered, including: weight to the nearest 0.1 kg using a digital scale, height to 0.1 cm via stadiometer and sitting height to the nearest 0.1 cm via stadiometer and chair. Sitting height values subtracted from height were used to define subischial limb length. Biomechanical data were gathered in the Wright State University three-dimensional motion analysis lab located at the Lifespan Health and Research Center (LHRC), and in the Wright State University department of Kinesiology and Health. The 3-D motion analysis system involves 6 high-speed Osprey cameras (Motion Analysis Corp.,

Santa Rosa, CA), which record data across a 15-meter walkway. To visualize sample data that were obtained from a gait analysis trial, please refer to figure 1.

The Helen Hayes set of retroreflective markers (Kadaba *et al* 1990), were used. Twenty-five retroreflective markers were placed on major joints and body segments by the same investigator bilaterally including: the mid-acromion process, the lateral epicondyles of the humerus, the middle of the wrist, left anterior superior iliac spine (ASIS) and right ASIS, lateral and medial femoral epicondyles, mid-shaft of the tibia, lateral and medial malleoli, heel, the head of the second metatarsal, and unilaterally on the sacrum (at the level of S1 on the sagittal midline). A static body position capture determined joint center location. All markers were used during static trials, while the medial femoral epicondyle and medial malleolus markers were removed before commencing dynamic walking trials. Data were discarded in the event of poor marker recognition. Kinematic data were obtained by Cortex 7.0 software's 3-dimensional system (Motion analysis Corp., Santa Rosa, CA), and processed by MacGait 1.0 (Motion analysis Corp., Santa Rosa, CA). Kinematic conventional directions were designated as the following: flexion was positive, extension past neutral was expressed as negative, adduction was positive and abduction was negative.

Figure 1.



The Helen Hayes set of retroreflective markers (Kadaba et al 1990) are visible in this image. The arrows represent GRF vectors. The subject is in double-limbed support in stance phase. Weight is being transferred from the lagging limb that is in toe-off to the leading limb as the forward step is imminent. Stance phase tends to last longer in KOA patients (Baliunas et al 2002); (Kubota et al 2007); (Teixeira & Olney, 1996), with knee flexion in this phase commonly being altered (Mandeville et al 2009).

Procedure

Intervention

Exercises were done twice a week for four weeks consistent with previously established frequency from protocol by Deyle *et al* 2005. Each session was an hour long. To ensure a consistent and complete stretch of anterior and posterior thigh muscles, Ely's test, Ober's test and SRL were administered to measure baseline muscle length. This baseline was used to confirm the patient is accessing the full stretch available (Gajdosik *et al* 1993).

Passive ROM exercises and active stretching were performed by a trained pre-physical therapy student on the affected and unaffected knee. To address muscle tightness, the prone quadriceps stretch and supine hamstring stretch were performed for a 30-second duration and frequency of 3 repetitions. The standing calf stretch also had a 30-second duration but was repeated 6 times. Passive ROM exercises included 6 repetitions of knee-extension with varus, 6 of knee-extension with valgus, and 6 flexions of the knee, each in 30-second durations.

An EZ Read Jamar® goniometer was used to gather flexion and extension ROM data. The goniometer's pivot was held at the lateral epicondyle of the femur with its proximal arm at the midline of the femur. The greater trochanter was used for orientation to approximate this midline. The distal arm was placed along the fibular midline, with the fibular head and lateral malleolus acting as reference points. The student applied the goniometer and read measurements, while Dr. Froehle recorded goniometer values and positioned limb segments appropriately. Flexion and extension measurements were taken with the subject prone, on both affected and unaffected knees, with patellas at the edge of the treatment table.

Walking Trials

Subjects initially rated their pain at rest using the Wong-Baker scale ("Wong Baker FACES foundation," n.d.)., then completed five walking trials. During walking trials, they were instructed to walk across a 15-meter walkway. They rated their pain after the fifth trial and again after the final appointment. Walking trials were self-paced to the speed most comfortable for the subject. To protect against falls, subjects were provided access to a harness and advised that they could stop walking trials at any time. Standard gait analysis was used to gather data of gait alterations before and after intervention.

Statistical analysis

The statistical analysis tests used to compare baseline (BL) variables to follow up (FU) values included one-tailed paired t-tests, Hedge's g, and common language effect size (CLES). Hedge's g also known as the corrected effect size, uses pooled weighted standard deviations to measure effect size and correct for bias in small sample populations. It is an appropriate indicator of effect-size for sample sizes less than 20, such as our cohort of seven subjects (Lakens, 2013). Statistical significance was set at $\alpha=0.10$ because of the limited statistical power of this small sample. For the same reason, we did not correct the p-value threshold for multiple comparisons.

III. RESULTS

Participant anthropometric measures (height and weight), BMI, KL grades, OA affected knee and sex are listed in table 1. Statistical analysis was done for the affected knee only. Of the 21 variables tested, the 6 highlighted in green in table 2 were effects of interest and changed significantly: walking speed, stride-length, cadence, peak knee flexion in stance, peak knee flexion in swing and knee flexion/extension (KFE) ROM in swing. Effects of interest are summarized in figures 2-7. The other variables did not change. Results for all the variables are summarized in table 2.

Sagittal plane kinematics

The baseline mean peak knee flexion in stance was 45.5° ± 6.4. The follow up mean peak knee flexion in stance was 50.0° ± 5.7. The p-value was 0.08. The Hedge's g value was 0.69. The CLES value was 0.73.

The baseline mean peak knee extension in swing was 5.5° ± 5.0. The follow up mean peak knee extension in swing was 6.6° ± 3.1. The p-value was 0.73. The Hedge's g value was 0.25. The CLES value was 0.60.

The baseline mean peak knee flexion in swing was 60.5° ± 4.5. The follow up mean peak knee flexion in swing was 63.7° ± 6.3. The p-value was 0.06. The Hedge's g value was 0.55. The CLES value was 0.76.

The baseline mean KFE ROM in stance was 37.5° ± 7.2. The follow up mean KFE ROM in stance was 40.0° ± 3.8. The p-value was 0.13. The Hedge's g value was 0.44. The CLES value was 0.68.

The baseline mean KFE ROM in swing was 55.1° ± 6.0. The follow up mean KFE ROM in swing was 57.1° ± 5.6. The p-value was 0.03. The Hedge's g value was 0.32. The CLES value was 0.80.

Frontal plane knee and hip kinematics

The baseline mean peak knee abduction in stance was -0.3° ± 4.1. The follow up mean peak knee abduction in stance was 0.9° ± 3.8. The p-value was 0.15. The Hedge's g value was 0.28. The CLES value was 0.58.

The baseline mean peak knee adduction in stance was 8.4° ± 5.7. The follow up mean peak knee adduction in stance was 8.3° ± 5.7. The p-value was 0.48. The Hedge's g value was 0.02. The Hedge's g value was 0.02. The CLES value was 0.51.

The baseline mean knee abduction and adduction ROM in stance was 8.7° ± 3.7. The follow up mean knee abduction and adduction ROM in stance was 7.4° ± 6.2. The p-value was 0.30. The Hedge's g value was 0.23. The CLES value was 0.58.

The baseline mean peak knee abduction in swing was 0.8° ± 3.2. The follow up mean peak knee abduction in swing was 1.0° ± 3.7. The p-value was 0.41. The Hedge's g value was 0.05. The CLES value was 0.52.

The baseline mean peak knee adduction in swing was 9.5° ± 7.1. The follow up mean peak knee adduction in swing was 8.7° ± 4.7. The p-value was 0.40. The Hedge's g value was 0.12. The CLES value was 0.54.

The baseline mean knee abduction and adduction ROM in swing was 8.7° ± 4.6. The follow up mean knee abduction and adduction ROM in swing was 7.7° ± 4.8. The p-value was 0.36. The Hedge's g value was 0.20. The CLES value was 0.57.

The baseline mean peak hip abduction in stance was -5.3° ± 6.0. The follow up mean peak hip abduction in stance was -5.6° ± 4.8. The p-value was 0.57. The Hedge's g value was 0.05. The CLES value was 0.53.

The baseline mean peak hip abduction in swing was -7.2° ± 5.0. The follow up mean peak hip abduction in swing was -6.6° ± 5.4. The p-value was 0.38. The Hedge's g value was 0.11. The CLES value was 0.55.

The baseline mean peak knee varus ω was 43.0°/s ± 24.6. The follow up mean peak knee varus ω was 49.5°/s ± 32.5. The p-value was 0.59. The Hedge's g value was 0.21. The CLES value was 0.61.

Spatiotemporal variables

Subjects had a baseline mean walking speed of 91.3 cm/s ± 20.8, and a follow up mean of 107.4 cm/s ± 11.4. The p-value was 0.07. The Hedge's g value was 0.89 and the CLES value was 0.76.

The baseline stride length mean was 114.7 cm ± 16.5. The follow up stride length mean was 120.4 cm ± 12.8. The p-value was 0.08. The Hedge's g value was 0.36. The CLES value was 0.76.

The baseline mean cadence of 96.0 steps/min., ± 17.7. Their follow up mean cadence was 107.5 steps/min ± 8.0. The p-value for cadence was 0.09. The Hedge's g value was 0.77. The CLES value was 0.73.

The baseline mean step width was 10.8 cm ± 3.0. The follow up mean step width measured 11.3 cm ± 3.9. The p-value was 0.63. The Hedge's g value was 0.13. The CLES value was 0.54.

The baseline single support duration mean was 36.4 %GC ± 2.6. The follow up single support duration mean was 36.4 %GC ± 3.5. The p-value was 0.4. The Hedge's g value was 0.00. The CLES value was 0.50.

The baseline stance phase duration mean was 63.3 %GC ± 3.4. The follow up stance phase duration mean was 61.2 %GC ± 7.9. The p-value was 0.28. The Hedge's g value was 0.31. The CLES value was 0.60.

Pain scores

With a p-value of 0.31, pain scores did not change significantly. Six out of seven subjects reported unchanged or lower pain at follow up. One subject reported higher pain at follow up compared to baseline. The median 5th trial pain score at baseline was 1, while the median 5th trial pain score at follow up was 0. Results for pain scores are summarized in table 3.

Table 1.

ID	Affected Side Left (L), Right (R)	KL Grade	Sex	Height (cm)	Weight (Kg)	BMI (kg/m^2)
CLN00001	L	2	F	162.4	97.0	36.8
CLN00003	R	3	F	165.6	109.7	40.0
CLN00004	L	2	F	173.2	80.8	26.9
CLN00005	R	2	M	163.5	79.3	29.7

CLN00006	L	2	F	152.0	71.8	31.1
CLN00007	L	3	F	168.0	90.7	32.1
CLN00009	L	2	F	164.0	90.0	33.5

Table 1. Participant anthropometric data, BMI, KL grades, OA affected knee and sex.

Table 2.

AFFECTED KNEE ONLY										
Variable	BL			FU			*T-test hypothesis*	*P***	*g****	CLES*****
	mean	±	sd	mean	±	sd				
Walking speed (cm/s)	91.3	±	20.8	107.4	±	11.4	FU > BL	0.07	0.89	0.76
Stride length (cm)	114.7	±	16.5	120.4	±	12.8	FU > BL	0.08	0.36	0.73
Cadence (steps/min)	96.0	±	17.7	107.5	±	8.0	FU > BL	0.09	0.77	0.73
Step width (cm)	10.8	±	3.0	11.3	±	3.9	FU < BL	0.63	0.13	0.54
Single support duration (%GC)	36.4	±	2.6	36.4	±	3.5	FU < BL	0.49	0.00	0.50
Stance phase duration (%GC)	63.3	±	3.4	61.2	±	7.9	FU < BL	0.28	0.31	0.60
Peak knee extension in stance (°)*	8.1	±	4.2	9.9	±	3.9	FU < BL	0.85	0.42	0.66
Peak knee flexion in stance (°)	45.5	±	6.4	50.0	±	5.7	FU > BL	0.08	0.69	0.73
KFE ROM in stance (°)	37.4	±	7.2	40.0	±	3.8	FU > BL	0.13	0.44	0.68
Peak knee extension in swing (°)	5.5	±	5.0	6.6	±	3.1	FU < BL	0.73	0.25	0.60
Peak knee flexion in swing (°)	60.5	±	4.5	63.7	±	6.3	FU > BL	0.06	0.55	0.76
KFE ROM in swing (°)	55.1	±	6.0	57.1	±	5.6	FU > BL	0.03	0.32	0.80
Peak knee abduction in stance (°)	-0.3	±	4.1	0.9	±	3.8	FU > BL	0.15	0.28	0.68
Peak knee adduction in stance (°)	8.4	±	5.7	8.3	±	5.7	FU < BL	0.48	0.02	0.51
KAbAd ROM in stance (°)	8.7	±	3.7	7.4	±	6.2	FU < BL	0.30	0.23	0.58
Peak knee abduction in swing (°)	0.8	±	3.2	1.0	±	3.7	FU > BL	0.41	0.05	0.52
Peak knee adduction in swing (°)	9.5	±	7.1	8.7	±	4.7	FU < BL	0.40	0.12	0.54
KAbAd ROM in swing (°)	8.7	±	4.6	7.7	±	4.8	FU < BL	0.36	0.20	0.57
Peak hip abduction in stance (°)	-5.3	±	6.0	-5.6	±	4.8	FU > BL	0.57	0.05	0.53
Peak hip abduction in swing (°)	-7.2	±	5.0	-6.6	±	5.4	FU > BL	0.38	0.11	0.55
Peak knee varus ω (°/s)	43.0	±	24.6	49.5	±	32.5	FU < BL	0.59	0.21	0.61

*Kinematic directional conventions are as follows: flexion: +; extension: −; adduction: +; abduction: −.

**One-tailed paired t-tests.

***Hedge's *g*, a measure of effect size for paired samples of continuous data.

****Common language effect size (probability of superiority/inferiority).

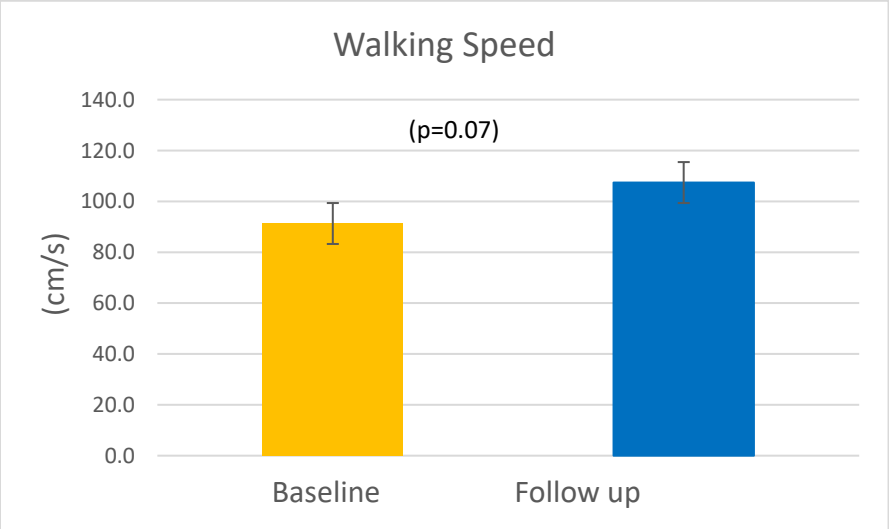
Table 2. Statistics results for all variables measured.

Table 3.

Subject	Pre	5th trial	Post		Pre	5th trial	Post
CLN00001	0	0	3		0	0	0
CLN00002							
CLN00003	0	1	1		0	1	2
CLN00004	3	4	4		2	0	0
CLN00005	0	0	0		0	0	0
CLN00006	0	0	0		0	0	0
CLN00007	4	2	2		0	0	0
CLN00008							
CLN00009	1	2	2.5		2	3	4

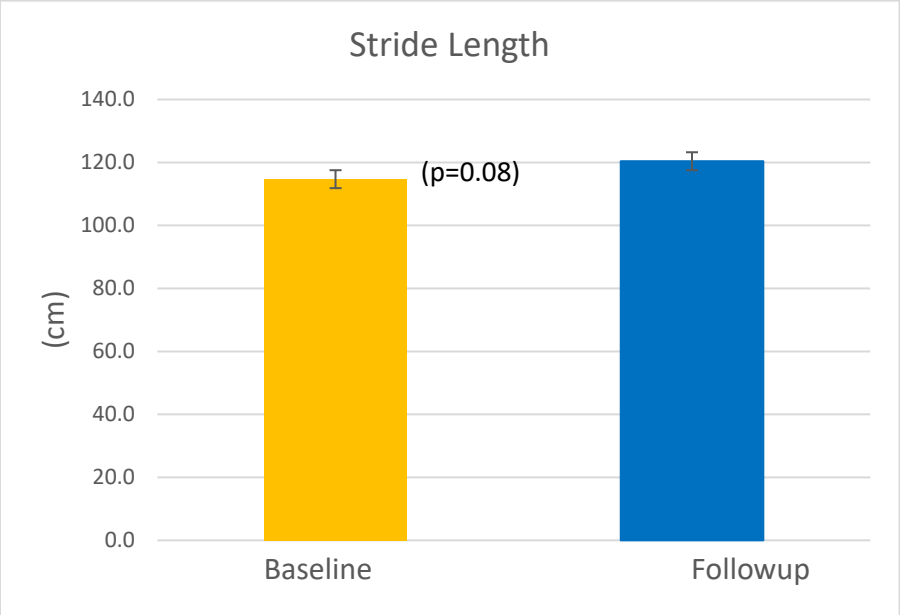
Table 3. Pain scores taken pre-intervention (pre), at the 5th trial, and post-intervention

Figure 2.



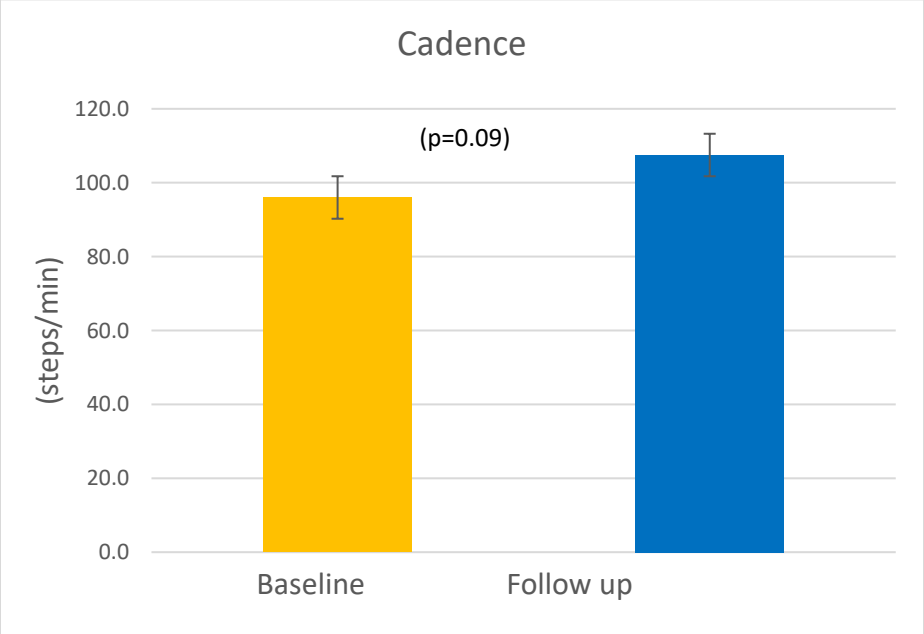
Each categorical bar represents the mean walking speed at baseline and follow up. Categories are measured in standard error bars.

Figure 3.



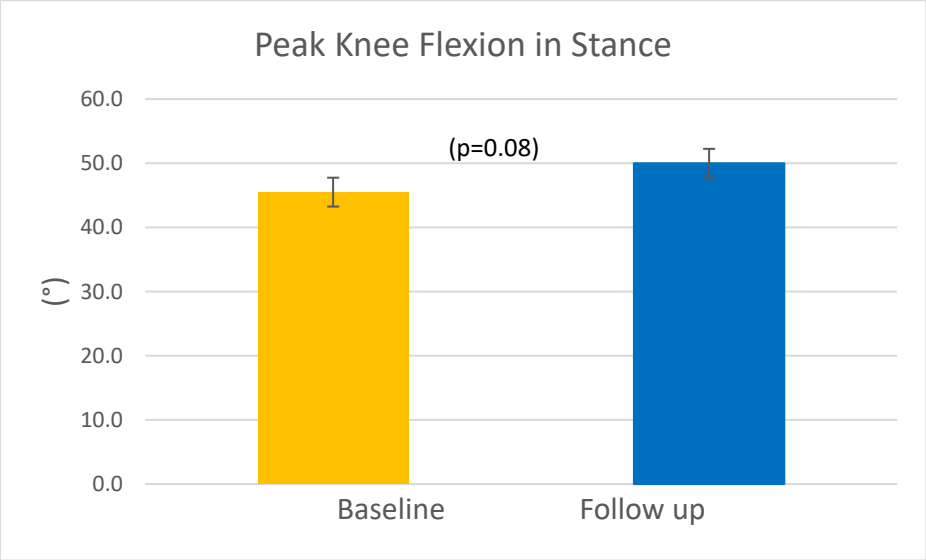
Each categorical bar represents the mean stride length at baseline and follow up. Categories are measured in standard error bars.

Figure 4.



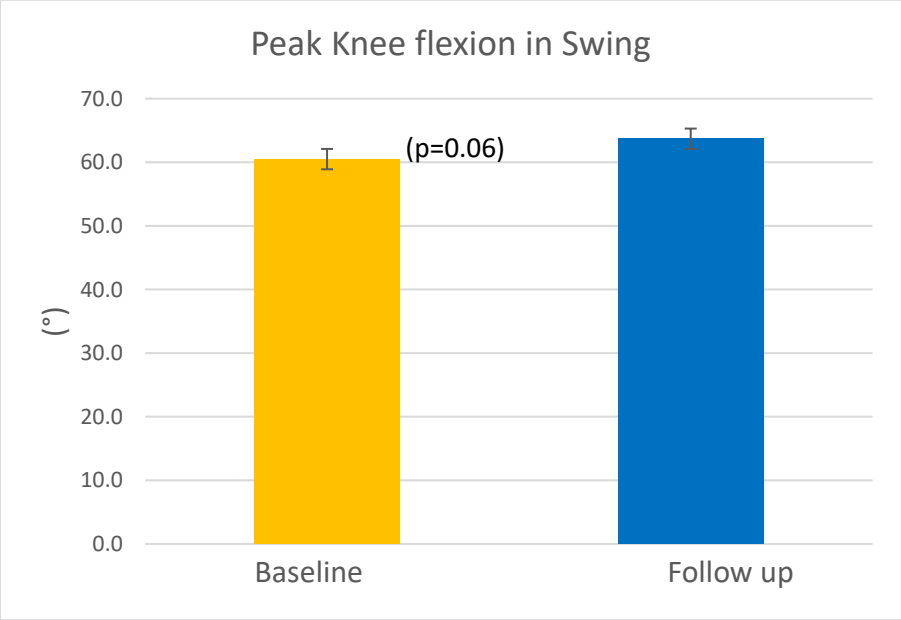
Each categorical bar represents the mean cadence at baseline and follow up. Categories are measured in standard error bars.

Figure 5.



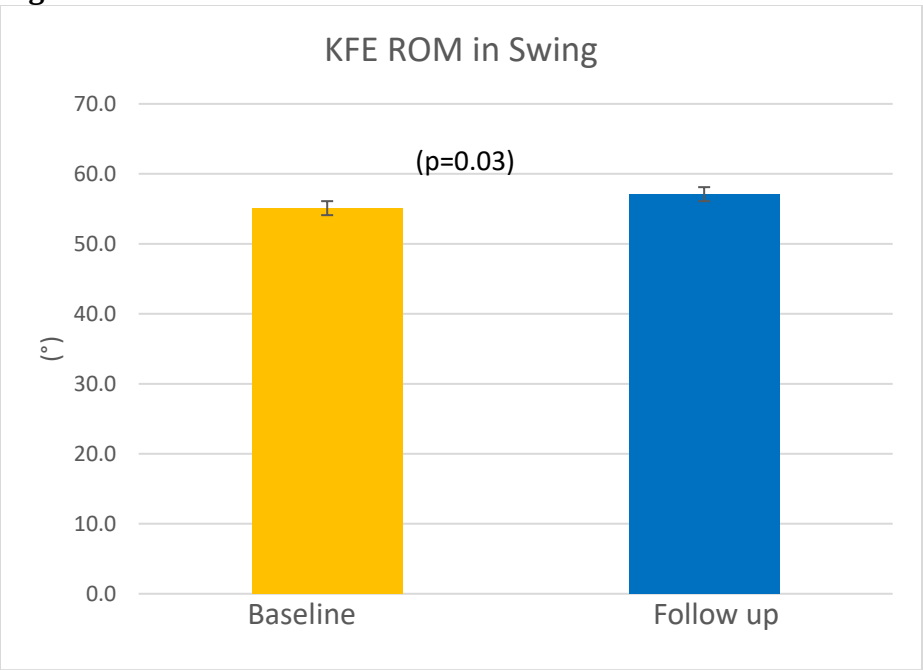
Each categorical bar represents the mean peak knee flexion in stance phase during baseline and follow up. Categories are measured in standard error bars.

Figure 6.



Each categorical bar represents the mean peak knee flexion in swing phase. Categories are measured in standard error bars.

Figure 7.



Each categorical bar represents the mean KFE ROM in swing phase. Categories are measured in standard error bars.

IV. DISCUSSION

The aim of this study was to examine how passive ROM and stretching affected early to mid-staged KOA patient gaits in terms of ROM and pain. Many studies have produced data on the advantages of exercise, particularly combined treatment modalities as therapeutic for non-surgical KOA subjects, with evidence of benefits in gait-speed increases, greater functionality and diminished pain. Our data supported the hypothesis that a combination of passive ROM and stretching would result in increased ROM and benefit patient gait. The intervention's pain results suggest that it was gentle enough to be tolerated as pain scores did not worsen by follow up, but did not support our second hypothesis that pain would be significantly decreased following therapy. The results of our research also supported past findings regarding knee ROM and improved gait from other exercise-based interventions.

Through all the spatiotemporal components used to classify gait, walking speed may be the strongest assessment of gait capacity (Neumann, 2010). KOA is known to slow gait (Ouellet & Moffet, 2002). Slow walking has many adverse general health-effects. While it may be a gait accommodation in KOA subjects, decreased walking speed may also act as a feed-back loop to complicate the disease by causing further deconditioning. A low gait speed reflects excess energy utilization in cardiopulmonary, circulatory and musculoskeletal systems, making it a clinical marker of multi-systemic damage. Decreased mobility due to low gait-speed can compound this energy loss by deconditioning multiple systems (Studenski *et al* 2011). Research of geriatric patients showed that a walking speed of $\leq$0.8 m/s doubled the diagnostic likelihood of qualifying as frail. Frailty is the collective term for a syndrome involving many adverse effects including but not limited to: a destabilized homeostatic reserve, increased vulnerability, muscle wasting, fall-risk, and likelihood of death (Castell *et al* 2013).

Studenski *et al* provided evidence of that a slow gait speed corresponds to diminished longevity. Statistical comparisons showed that patients who had a gait of ≥1.0 m/s lived longer than expected, compared to predicted longevity based solely on age or sex. C-statistics for gait-speed, age and sex had a greater five-year survival predictability than those for chronic disease, age and sex in 4 out of 9 studies. Cesari *et al* also produced data supporting a cut-off point gait speed of <1.0 m/s as an indicator of high-risk health outcomes. Harmful prognostic outcomes associated with this gait speed included persistent severe lower extremity limitation, meaning two self-reports of difficulty or inability to walk a quarter of a mile or climb 10 steps without resting, (rate ratio 2.20, 95% confidence interval), hospitalization (rate ratio 1.48, 95% confidence interval), and death (rate ratio 1.64, 95% confidence interval.). The health consequences of slow gait may increase morbidity for KOA patients (Felson, 2009).

A common area of improved functionality among KOA patients who participate in exercise programs is increased gait speed (Jansen *et al* 2011). Our results of improved gait speed are consistent with those from other studies. For example, a combination of exercise and stretching in a study by Røgind *et al* 1998, resulted in increased walking speed by 13% in KOA subjects, and a program of stretching and passive ROM by Falconer *et al* 1992 found that 72% of KOA patients showed a rise in gait velocity. Subjects from our study started the intervention with a baseline mean walking speed of 91.3 ± 20.8 cm/s and at follow up, had a mean walking speed of 107.4 ± 11.4 cm/s. The high CLES value (0.76) and the low p-value (p=0.07) associated with this change suggest that the intervention had a strong effect on gait speed in subjects. The high Hedge's g value (0.89) is further support of the large effect size.

Aside from speed deficits, cadence, and stride length deficits are also significantly affected in KOA gait pathology (Ouellet & Moffet 2002). These variables should directly affect

each-other, i.e. the greater the stride length and cadence, the greater the speed (Whittle, 2008). This relationship was consistent with the results of our study, with moderate to large increases in stride length and cadence corresponding with increased gait speed. Patient baseline mean stride length was 114.7 ± 16.5 cm, and increased to 120.4 ± 12.8 cm. This increase was significant (p=0.08), CLES = 0.73, g = 0.36. Their cadence began at a baseline mean of 96.0 ± 17.7 steps/min and rose to 107.5 ± 8.0 steps/min at follow up, with a significance of (p=0.09), CLES= 0.73, g=0.77. Gait speed, cadence and stride-length increases all suggest increased knee flexibility.

Other exercise-based interventions have yielded similar results of increased knee mobility, decreased stiffness and greater knee ROM. In past exercise-therapy studies, post-intervention KOA subjects expressed greater knee flexibility in functional improvements such as gait-speed increases, increased distance covered during walking trials, and decreased time required to ascend stairs (Schilke *et al* 1996; Røgind *et al* 1998; Petrella & Bartha, 2000; Deyle *et al* 2005). If knee flexibility increased in our subjects, it should be supported by results of greater overall ROM and increased knee flexion during the swing phase and stance phase of the gait cycle.

Our findings are that KFE-ROM during swing and peak knee flexion during swing both increased significantly, indicating increased knee flexibility post-intervention. Baseline mean KFE-ROM in swing for subjects was 55.1 ± 6.0˚ and increased to a follow up mean of 57.1 ± 5.6˚, (p=0.03), CLES=0.80, g=0.32. Peak knee flexion during swing changed from a baseline mean of 60.5 ± 4.5˚ versus a follow up mean of 63.7 ± 6.3˚, (p=0.06), CLES=0.76, g=0.55. The pivotal moment during swing that allows for ambulation and forward motion is ground-clearance, which in normal motion, relies heavily on knee flexion. An increase in KFE-ROM

during swing and a greater peak knee flexion during swing, implies that subjects have improved ground clearance. Their flexion and ROM for the swing limb is greater. Improved clearance is dependent in part, on greater knee flexibility. Subject mean peak knee flexion in stance was also increased, which lends support to increased knee flexibility.

Subjects began with a baseline mean peak knee flexion in stance of 45.5 ± 6.4˚ compared to a follow up mean of 50.0 ± 5.7˚, (p=0.08), CLES=0.73, g=0.69. Knee flexion occurs at the end of stance, where the heel is being raised off the ground towards toe-off, in preparation for the ground clearance that will happen during swing (Neumann, 2010). A stance-phase increased mean peak knee flexion value at follow up suggests that participants have improved their capacity to flex their knees prior to clearance.

While Deyle *et al* 2005 used different primary outcome measures that did not include gait analysis or goniometry, comparisons for their findings can still be made with our study. Both exercise groups from the Deyle *et al* 2005 study experienced a 10% increase in walking distance during their 6-minute walking test, from baseline to follow up. They increased the amount of distance they were able to cover over time, meaning they increased their gait speed. Our results showed an 18% increase in walking speed consistent with their results.

The KL grade of our patients generally matched that of the Deyle *et al* 2005 work. The majority of their clinic subjects (41%), were KL grade 2. Of our subject population, 71% were KL grade 2. Given that disease severity was similar among both populations, it is reasonable to extrapolate that exercise therapy would have a similar effect on both cohorts. Their clinic group is more comparable to our participants in that the interventions were similar. The duration of intervention between Deyle *et al* 2005 and our study were also the same, 8 sessions over 4 weeks. Unlike the clinic group in the 2005 study, our subjects did not receive Maitland

Mobilization, perform strengthening exercises or active ROM. Our subjects were also not instructed to perform a daily walking regimen.

KOA subjects have been shown to have hip and leg muscle weakness which may contribute to gait changes (Lun *et al* 2015). Because the Deyle *et al* 2005 clinic group and the home group each performed strengthening exercises, it is possible that their increases in gait speed came from increased muscle strength. However, evidence produced by our study suggests otherwise, as our subjects did not perform active strengthening exercises and still experienced slightly higher increases in gait speed.

In our study, hip abduction in stance and swing did not change significantly from baseline to follow up. Weakness compromises hip abductors in KOA affected subjects. As hip abduction is required for stabilization during gait and for single-limb support, it is often relied upon as a form of gait compensation (Bennell *et al* 2010). Because hip abduction didn't change from baseline, it is likely that patients never compensated through the hip. A change in gait probably wasn't required because of the early-mid KL grade of the subjects. Their compensation for pain during gait took the form of slowed gait speed. This is a common walking adaptation seen in KOA individuals across KL-grades, with walking speed decreasing as KL-grades increase (White *et al* 2013).

Step width and single support duration, each of which are required for frontal plane stability, did not change. When step width and single support times increase, it is a sign that the patient is compensating. Had these values decreased from baseline to follow-up, it would be evidence of improved stability (Neumann, 2010). These data did not change which is evidence that patients did not yet require a gait change of this nature because of the early grading of their KOA.

Another set of variables that did not change were the angular velocities and ROM variables in the frontal plane. The intervention focused on motion in the sagittal plane (flexion and extension) which are major functional components in gait and components strongly affected by KOA. We also did not include correcting mechanisms for malalignment or joint-space-narrowing which would have likely altered frontal plane motion. The only frontal plane motion mildly addressed were the additions of varus and valgus pressure included during passive ROM extension and it is not surprising that those minor motions did not affect overall frontal plane dynamics.

It is encouraging that our study yielded similar gait improvement results to the Deyle *et al* 2005 study despite the simplification of our treatment modalities. Our subjects did not undergo strength-training, daily walking programs, Maitland mobilization or active ROM, but still experienced benefits in gait speed, stride-length, cadence, peak knee flexion in stance and greater swing limb reach. An advantage of our method is that a simplified treatment model is more likely to be followed by patients than complex protocol (Becker, 1985).

The protocol of our study paralleled work by Deyle and colleagues in that it involved supervision. The guidance of a clinic setting may have contributed to subject improvement in our study and the clinic group from theirs. According to research by Jette *et al* 1982, between 45-60% of arthritis patients do not adhere to prescribed exercise programs. Under supervision, patient compliance is more likely (Becker, 1985). Corrections can be made to exercise techniques under supervision ensuring patients can receive the maximum benefit from therapy. Supervision is also advantageous because feedback is encouraging to patients, making them less likely to drop out of the intervention (Haynes *et al* 1987). Guidance in a clinic setting also allows for patient-education. Management of a chronic illness requires a subject to be informed about

what exacerbates or helps disease symptoms. One study found that 90% of KOA patients received no education about arthritis management (Shim *et al* 2018). An advantage of a supervised intervention is that patients can be educated about how exercise can improve functionality and coached on how to maintain an active lifestyle.

Another advantage of passive ROM and supervised exercise over home exercise programs is that the exercises can be tailored to suit patient requirements and subjects can be monitored for adverse effects. In the study by Deyle *et al* 2005, participants were examined at each clinic visit for signs of inflammation (increased pain, effusions or heat over the affected joint). Therapy was continued only if those signs diminished. If a subject experienced soreness of a duration spanning more than a few hours, therapy was decreased as needed. These kinds of modifications are applicable to patients at later stages of OA.

Passive exercise and stretching is advantageous because it is more accessible to patients with increased levels of disability and pain. Our intervention was well-tolerated based on pain reports not having worsened. The results of our pain data were that patient pain was unchanged from baseline to follow up. Six out of seven subjects reported unchanged or lower pain at follow up. Had the intervention proved detrimental, patients would have reflected that intolerance in worsened pain scores.

Individuals with increased KL grades will not tolerate active exercises such as strengthening exercises that would be tolerable for mild to moderate KOA groups. Severe KOA patients may exhibit quadriceps weakness, and/or poor quadriceps muscle activation, suffer higher pain, joint instability, or knee laxity which have been shown to limit rehabilitation responses and compliance in exercise programs, including those that are focused on strengthening muscle groups (Fitzgerald, 2005). However, guided therapy such as those used

during our intervention may prove accessible to patients with higher KL grades because they are supervised and involve a treatment table.

High surfaces are recommended (chairs on blocks, elevated toilet seats and shower-chairs as opposed to bath-tubs), as a form of joint protection in severe KOA (Brandt, 2001). Treatment tables, as they are high off the ground, would also be categorized as more accessible for severe KOA patients. Low surfaces also pose fall risks with the pain of knee extension upon a sit-to-stand-transfer or flexion during squatting (Brandt, 2001). Passive ROM and other gentle forms of guided physical therapy on treatment tables such as those used in our intervention may protect the knee from further damage and decrease energy expenditure and so may prove more tolerable for severe KOA patients. There is less pain in a transfer such as moving to and from a treatment table as it does not involve heavy knee extension. With knee pain being the strongest discouragement to lower extremity functional increase in KOA patients (Jordan *et al* 1997), interventions such as ours that use treatment tables may be more likely to be completed in KOA patients who suffer a high amount of pain. The presence of a rehabilitation therapist has the added benefit of confidence building, by providing an unsteady KOA patient with assistance during transfers, exercise performance and ambulation. As many KOA patients struggle with fears of physical activity-induced pain and fear of ability to successfully perform physical activities (Fitzgerald, 2005), a confident subject is more likely to comply with and complete exercise therapy.

Limitations to the study

Our small sample size was a limiting factor. Recruitment issues meant that our subject population may not adequately reflect the effect of therapy. Future studies would benefit from an

increased sample size to see if gait improvements such as gait-speed and KFE-ROM would increase consistently and maintain effect size. Another result of the small sample size was the homogenous group of subjects based on sex. Because our subject population was primarily female, it is possible that subject sex could have affected our results. Women have more accelerated KOA progression than men (Brandt, 2001). The width of the female pelvis can predispose her knees to valgus alignment, which may alter gait patterns and their associated data. A cohort of subjects that were equally proportioned by sex would provide reliable data that would account for this potential difference. It is also possible that subjects in our study developed gait improvements unrelated to the applied intervention. Bonds between physical therapist and patient over extended treatment periods have been cited as a potential influence for subject improvement. This is a limit of supervised exercise, as home exercise groups would not have that influence as a confounding variable. It is unlikely that this kind of placebo effect would develop and trigger a change in subjects over the span of a month.

Time was another limiting factor. Exercise-based interventions on KOA trialed for longer periods in literature span from 12 weeks to 18 months. Trials with extended time may yield different results. Related to time is frequency of interventions. Extended trials have more opportunities for implementing exercises more frequently which may affect outcomes. Increased frequency would require closer patient-monitoring because longer studies such as the one by Røgind *et al* 1998 that lasted 3 months, bi-weekly in frequency, resulted in palpable effusions. Patients from that study were staged as severe KOA, so it is possible that increased exercise duration and frequency would be better tolerated by early to mid-KOA subjects. Despite limited time and a less complex procedure, our study is promising in that it yielded functional changes

without requiring a duration as extensive as other KOA rehabilitation studies and was simple to perform.

We did not have access to the WOMAC scale, though it would benefit future research if subjects were scored by the standard for pain. With these data scored in a way that is consistent with other KOA research, it is easier to notice trends that correlate with other findings. We encountered the same dilemma with PQAS. More advanced tests may produce different data.

A longer period to gather follow up data after the intervention was complete would provide more insight to the impact of treatment and how effects changed over time. While our study did collect follow up data after the intervention, time constraints did not allow follow up data collection over years, compared to other, larger studies that had the luxury of longevity. This is clinically relevant because of the chronic nature of OA. Not only would gathering follow up data over a longer time-span post-intervention enhance our understanding of how improvements change or remain over time, it would provide an opportunity to monitor subject disease progression through other treatments, such as how many of the cohort required invasive treatment, surgical intervention or how many subjects experienced delayed TKA, or were able to forego intraarticular injections.

Future Studies

Data from this research will contribute to the on-going longitudinal project of developing an OA pain-index. This intervention has clinical relevance as it is an uncomplicated treatment applicable for early stage non-surgical candidates that has shown promising effects on ROM and gait-speed. These methods are also gentle enough to be applied to inpatients or outpatients. Collected data can be applied to longitudinal current studies of OA or can serve as a foundation

for further studies such as those involving KOA and gait-alterations and be compared or combined with other pain-relief interventions. Finally, the information gathered is applicable to multiple fields, from rheumatology, to pain-management, physiatry, orthopedics and biomechanics.

Conclusions

The results of our study support our hypothesis that patient ROM would increase and gait would improve in response to passive ROM and stretching exercise therapy. Pain scores did not decrease significantly in response to therapy, so our hypothesis about pain being significantly altered was not supported. Based on our results, the following conclusions can be made:

- Significant improvement in knee ROM and gait speed is achievable for KOA patients even under short-duration exercise interventions.
- KOA patient knee ROM and gait speed can significantly increase in simplified models of exercise therapy.
- KOA pain is not worsened by a passive ROM and stretch-based therapeutic intervention.

V. REFERENCES

Altman, R., Asch, E., Bloch, D., Bole, G., Borenstein, D., Brandt, K., …Wolfe, F. (1986). Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum, 29*(8), 1039–1049.

American Thoracic Society. (2002). ATS Statement: Guidelines for the Six-Minute Walk Test. https://www.thoracic.org/statements/resources/pfet/sixminute.pdf

Astephen, J. L., Deluzio K. J., Caldwell, G. E., & Dunbar, M. J. (2008). Biomechanical changes at the hip, knee, and ankle joints during gait are associated with knee osteoarthritis severity. *J Orthop Res, 26*(3), 332-341.

Ayral, X., Pickering, E. H., Woodworth, T. G., Mackillop, N., & Dougados, M. (2005). Synovitis: a potential predictive factor of structural progression of medial tibiofemoral knee osteoarthritis – results of a 1-year longitudinal arthroscopic study in 422 patients. *Osteoarthritis and Cartilage, 13*(5), 361-367.

Baker, K. R., Nelson, M. E., Felson, D. T., Layne, J. E., Sarno, R., & Roubenoff, R. (2001). The efficacy of home based progressive strength training in older adults with knee osteoarthritis: A randomized controlled trial. *J Rheumatol, 28*(7), 1655-1665.

Baliunas, A. J., Hurwitz, D. E., Ryals, A. B., Karrar A., Case, J. P., Block, J. A., & Andriacchi, T. P. (2002). Increased knee joint loads during walking are present in subjects with knee osteoarthritis. *Osteoarthritis Cartilage, 10*(7), 573–579.

Bautch, J.C., Malone, D.G. & Vailas, A.C. (1997), Effects of exercise on knee joints with osteoarthritis: A pilot study of biologic markers. *Arthritis & Rheumatism, 10*(1), 48-55. doi:10.1002/art.1790100108

Beal, M. D., Delagrammaticas, D., & Fitz, D. (2016). Improving outcomes in total knee arthroplasty—Do navigation or customized implants have a role? *J Orthop Surg Res, 11***(**60). doi:10.1186/s13018-016-0396-8

Becker, M. H. (1985). Patient adherence to prescribed therapies. *Medical care, 23*(5), 539-555.

Bennell, K., Hunt, M., Wrigley, T., Hunter, D., Mcmanus F., Hodges, P., . . . Hinman, R. (2010). Hip strengthening reduces symptoms but not knee load in people with medial knee osteoarthritis and varus malalignment: a randomised controlled trial. *Osteoarthritis and Cartilage, 18*(5), 621-628. doi:10.1016/j.joca.2010.01.010

Brandt, K. D. (2001). *The encyclopedia of visual medicine series: An atlas of osteoarthritis.* (pp. 6, 7, 13, 20, 25, 26, 67, 83, 89). Pearl River, NY: The Parthenon Publishing Group.

Brandt, K. D. (2005). Osteoarthritis. In Harrison, T. R., Kasper, D. L., Braunwald, E., Fauci, A., Longo, D., Hauser, S. L., & Jameson, J. L. (Eds.), *Harrison's Principles of Internal Medicine* (16th ed., pp. 2038-2040). (Vol 2), New York City, NY: McGraw-Hill, Medical Pub. Division.

Braun, H. J., & Gold, G. E. (2012). Diagnosis of osteoarthritis: imaging. *Bone, 51*(2), 278–288. doi:10.1016/j.bone.2011.11.019

Castell, M., Sánchez, M., Julián, R., Queipo, R., Martin, S., & Otero, A. (2013). Frailty prevalence and slow walking speed in persons age 65 and older: implications for primary care. *BMC Fam Pract, 14*(86). doi:10.1186/1471-2296-14-86

Chamberlain, M. A., Care, G., & Harfield, B. (1982). Physiotherapy in osteoarthritis of the knees. A controlled trial of hospital versus home exercises. *Int Rehabil Med, 4*(2), 101-106.

Cesari, M., Kritchevsky, S. B., Penninx, B.W., Nicklas, B. J., Simonsick, E. M., Newman, A.B.; Tylavsky, F.A….Pahor, M. (2005). Prognostic value of usual gait speed in well-functioning older people—Results from the health, aging and body composition study. *J. Am. Geriatr. Soc, 53*(10), 1675–1680.

Chang, A., Hayes, K., Dunlop, D., Hurwitz, D., Song, J., Cahue, S., …Sharma, L. (2004). Thrust during ambulation and the progression of knee osteoarthritis. *Arthritis & Rheumatism, 50*(20), 3897–3903. doi:10.1002/art.20657

D'Ambrosia, R. D. (2005). Epidemiology of Osteoarthritis. *Orthopedics, 28*(*Suppl*. 2), 201-205.

DeLisa, J. A., Gans, B. M., & Walsh, N. E. (2007). *Delisa's physical medicine and rehabilitation: Principles and practice*. (5th ed.). (Vol 1, pp. 121-127, 1680). Philadelphia, PA: Lippincot Williams and Wilkins.

Deyle, G. D., Allison, S. C., Matekel, R. L., Ryder, M. G., Stang, J. M., Gohdes, D. D., … Garber, M. B. (2005). Physical therapy treatment effectiveness for osteoarthritis of the knee: A randomized comparison of supervised clinical exercise and manual therapy procedures versus a home exercise program. *Journal of American Physical Therapy Association, 85*(12), 1301-1317.

Ettinger, W. H., Burns, R., Messier, S. P., Applegate, W., Rejeski. W. J., Morgan, T., …Craven, T. (1997). A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis: The fitness arthritis and seniors trial (FAST). *JAMA, 277*(1), 25–31. doi:10.1001/jama.1997.03540250033028

Falconer, J., Hayes, K. W., & Chang, R. W. (1992). Effect of ultrasound on mobility in osteoarthritis of the knee: A randomized clinical trial. *Arthritis Care Res, 5*(1), 29-35. doi: 10.1002/art.1790050108

Favre, J., & Jolles, B. M. (2017). Gait analysis of patients with knee osteoarthritis highlights a pathological mechanical pathway and provides a basis for therapeutic interventions. *EFORT open reviews*, *1*(10), 368–374. doi:10.1302/2058-5241.1.000051

Felson, D. T., Lawrence, R. C., Dieppe, P. A., Hirsch, R., Helmick, C. G., Jordan, J. M., …Fries, J. F. (2000). Osteoarthritis: new insights. Part 1: the disease and its risk factors. *Ann Intern Med, 133*(8), 635-646.

Felson, D. T. (2009). Developments in the clinical understanding of osteoarthritis. *Arthritis Research & Therapy*, *11*(1), 203. doi:10.1186/ar2531

Fisher, N. M., Pendergast, D. R., Gresham, G. E., & Calkins, E. (1991). Muscle rehabilitation: Its effect on muscular and functional performance of patients with knee osteoarthritis. *Arch Phys Med Rehabil*, *72*(6), 367-374.

Fisher, N. M., Gresham, G. E., Abrams, M., Hicks, J., Horrigan, D., Pendergast, D. R. (1993). Quantitative effects of physical therapy on muscular and functional performance in subjects with osteoarthritis of the knees. *Arch Phys Med Rehabil*, *74*(8), 840-851.

Fitzgerald, G. K. (2005). Therapeutic exercise for knee osteoarthritis: Considering factors that may influence outcome. *EUR MEDICOPHYS*, *41*(2), 163-171.

Fransen, M., Crosbie, J., & Edmonds, J. (2001). Physical therapy is effective for patients with osteoarthritis of the knee: A randomized controlled clinical trial. *J Rheumatol, 28*(1), 156-164.

Fransen, M., McConnell, S., & Bell, M. (2002). Therapeutic exercise for people with osteoarthritis of the hip or knee. A systematic review. *The Journal of rheumatology*, *29*(8), 1737-1745.

Gajdosik, R. L., Rieck, M. A., Sullivan, D. K., & Wightman, S. E. (1993). Comparison of four clinical tests for assessing hamstring muscle length. *Journal of Orthopaedic & Sports Physical Therapy, 18*(5), 614-618. doi:10.2519/jospt.1993.18.5.614

Gudbergsen, H., Lohmander, L., Jones, G., Christensen, R., Danneskiold-Samsøe, B., Bliddal, H., & Boesen, M. (2013). Correlations between radiographic assessments and MRI features of knee osteoarthritis—A cross-sectional study. *Osteoarthritis Cartilage, 21*(4), 535-543. doi: 10.1016/j.joca.2012.12.010.

Hall, C. M., & Brody, L. T. (2005). *Therapeutic exercise: Moving toward function*. (pp. 75-78). Philadelphia: Lippincott Williams & Wilkins.

Hehne, H. J. (1990). Biomechanics of the patellofemoral joint and its clinical relevance. *Clin Orthop,* 258, 73-85.

Hinman, R. S., Hunt, M. A., Creaby, M. W., Wrigley, T. V., McManus, F. J., & Bennell, K. L. (2010). Hip muscle weakness in individuals with medial knee osteoarthritis. *Arthritis Care Res*, *62*(8), 1190-1193.

Hopman-Rock, M., & Westhoff, M. H. (2000). The effects of a health educational and exercise program for older adults with osteoarthritis for the hip or knee. *J Rheumatol*, *27*(8), 1947-1954.

Hunter, D. J., McDougall, J. J., & Keefe, F. J. (2008). The symptoms of osteoarthritis and the genesis of pain. *Rheumatic diseases clinics of North America*, *34*(3), 623–643. doi:10.1016/j.rdc.2008.05.004

Hurwitz, D.E., Ryals, A.B., Case, J.P., Block, J.A. & Andriacchi, T.P. (2002). 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*, *20*(1), 101-107. doi:10.1016/S0736-0266(01)00081-X

Jansen, M. J., Viechtbauer, W., Lenssen, A. F., Hendriks, E. J., & de Bie, R. A. (2011). Strength training alone, exercise therapy alone, and exercise therapy with passive manual mobilisation each reduce pain and disability in people with knee osteoarthritis: A systematic review, J Physiother, *57*(1), 11-20.

Jette, A. M. (1982). Improving patient cooperation with arthritis treatment regimens. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, *25*(4), 447-453.

Johnson, V. L., & Hunter, D. J. (2014). The epidemiology of osteoarthritis. *Best Pract Res Clin Rheumato*, *28*(1), 5–15.

Jones, R. K., Chapman, G. J., Findlow, A. H., Forsythe, L., Parkes, M. J., Sultan, J., & Felson, D. T. (2013). A new approach to prevention of knee osteoarthritis: Reducing medial load in the contralateral knee. *Journal of Rheumatology, (40)*3, 309-315. doi: 10.3899/jrheum.120589

Jordan, J., Luta, G., Renner, J., Dragomir, A., Hochberg, M., & Fryer, J. (1997). Knee pain and knee osteoarthritis severity in self-reported task specific disability: the Johnston County Osteoarthritis Project. *The Journal of rheumatology*, *24*(7), 1344-1349.

Kadaba, M. P., Ramakrishnan, H. K., & Wootten, M. E. (1990). Measurement of lower extremity kinematics during level walking. *J Orthop Res*, *8*(3), 383-392

Kaufman, K. R., Hughes, C., Morrey, B. F., Morrey, M., & An, K. N. (2001) Gait characteristics of patients with knee osteoarthritis. *J Biomech*, *34*(7), 907-915. doi: 10.1016/S0021-9290(01)00036-7

Kohn, M. D., Sassoon, A. A., & Navin, D. F. (2016). Classifications in brief: Kellgren-Lawrence classification of osteoarthritis. *Clinical Orthopaedics and Related Research, 474*(8), 1886.

Komdeur, P., Pollo, F. E., & Jackson, R. W. (2002). Dynamic knee motion in anterior cruciate impairment: a report and case study. *Proceedings (Baylor University. Medical Center), 15*(3), 257–259. doi:10.1080/08998280.2002.11927850

Kovar, P. A., Allegrante, J. P., MacKenzie, C. R., Peterson, M. G., Gutin, B., & Charlson, M. E. (1992). Supervised fitness walking in patients with osteoarthritis of the knee: A randomized, controlled trial. *Ann Intern Med*. 116(7), 529–534. doi: https://doi.org/10.7326/0003-4819-116-7-529

Kubota, M., Shimada, S., Kobayashi, S., Sasaki, S., Kitade, I., Matsumura, M., …Baba, H. (2007). Quantitative gait analysis of patients with bilateral hip osteoarthritis excluding the influence of walking speed. *J Orthop Sci*, *12*(5), 451–457.

Lakens, D. (2013). Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. *Frontiers in psychology*, *4*, 863.

Liikavainio, T., Lyytinen, T., Tyrväinen, E., Sipilä, S., & Arokoski, J. P. (2006). Physical function and properties of quadriceps femoris muscle in men with knee osteoarthritis. *Archives of Physical Medicine and Rehabilitation, 89*(11), 2185 – 2194.

Lohman, T. G., Roche, A. F., & Martorell, R. (1988). *Anthropometric standardization reference manual* (Vol. 177, pp. 3-8). Champaign, IL: Human kinetics books.

Losina, E., Silva, G. S., Smith, K. C., Collins, J. E., Hunter, D. J., Shrestha, S., ... & Katz, J. N. (2019). Quality-Adjusted Life-Years Lost Due to Physical Inactivity in the United States Osteoarthritis Population. *Arthritis care & research*.

Lun, V., Marsh, A., Bray, R., Lindsay, D., & Wiley, P. (2015). Efficacy of hip strengthening exercises compared with leg strengthening exercises on knee pain, function, and quality of life in patients with knee osteoarthritis. *Clin J Sport Med, (25)*6, 509-517. doi:10.1097/jsm.0000000000000170

Magee, D. J., Zachazewski, J. E., & Quillen, W. S. (2009). *Pathology and intervention in musculoskeletal rehabilitation.* (pp. 870). St. Louis, MO: Elsevier.

Malanga, G., & Delisa, J. A. (1998). Gait Analysis in the Science of Rehabilitation, Section 1: Clinical Observation [Monograph]. *U.S. Department of Veterans Affairs, Veterans Health Administration, R.RD.S., 2,* 1-10. https://ia600206.us.archive.org/6/items/gaitanalysisinsc00joel/gaitanalysisinsc00joel.pdf

Mandeville, D., Osternig, L. R. & Chou, L. S. (2009). The associations between knee flexion, vertical center of mass excursions and lower extremity muscle work for end stage knee osteoarthritis. *Journal of Musculoskeletal Research, (12)*2, 77-84.

Mathiessen, A., & Conaghan, P.G. (2017) Synovitis in osteoarthritis: Current understanding with therapeutic implications. *Arthritis Res Ther, 19*(1), 18. https://doi.org/10.1186/s13075-017-1229-9

Miller, P. K., & Bird, A. M. (1976). Localized muscle fatigue and dynamic balance. *Percept Mot Skills, 42*(1), 135-138.

Mills, K., Hunt, M. A., & Ferber, R. (2013). Biomechanical deviations during level walking associated with knee osteoarthritis: A systematic review and meta-analysis. *Arthritis Care Res, 65*(10), 1643-1665.

Minor, M. (1994). Exercise in the management of osteoarthritis of the knee and hip. *Arthritis Care Res, 7*(4), 198-204.

Miyazaki, T., Wada, M., Kawahara, H., Sato, M., Baba, H., & Shimada, S. (2002). Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. *Annals of the rheumatic diseases, 61*(7), 617–622. doi:10.1136/ard.61.7.617

Moore, K. L., Dalley, A. F., & Agur, A. M. R. (2014). *Clinically oriented anatomy*. (7th ed.). (pp. 25, 545-550, 570, 597, 634-642). Philadelphia, PA: Lippincott Williams & Wilkins.

Mündermann, A., Dyrby, C. O., Hurwitz, D. E., Sharma, L., & Andriacchi, T. P. (2004). Potential strategies to reduce medial compartment loading in patients with knee osteoarthritis of varying severity: Reduced walking speed. *Arthritis and Rheumatism, 50*(4), 1172-1178. doi:10.1002/art.20132

Myers, S. L. (2004). Osteoarthritis and crystal-associated synovitis. In G. G. Hunter (Ed.), *Atlas of rheumatology* (4th ed., pp. 54-68). Philadelphia, PA: Current Medicine LLC.

Neumann, D. A. (2010). *Kinesiology of the musculoskeletal system: Foundations for rehabilitation.* (2nd ed.). (pp. 5, 7, 501, 520, 521, 527, 531, 533, 632). St. Louis, MO: Mosby Elsevier.

Nordin, M., & Frankel, V. H. (2001). *Basic biomechanics of the musculoskeletal system*. (pp. 4, 195, 452). Philadelphia, PA: Lippincott Williams & Wilkins.

Noyes, F. (2017). *Noyes' knee disorders: Surgery, rehabilitation, clinical outcomes.* (2nd ed.). (pp. 126-127). Philadelphia, PA: Saunders, Elsevier.

O'Reilly, S. C., Muir, K. R., & Doherty, M., (1999). Effectiveness of home exercise on pain and disability from osteoarthritis of the knee: A randomised controlled trial. *Annals of the Rheumatic Diseases, 58*(1), 15-19.

Ouellet, D., & Moffet, H. (2002). Locomotor deficits before and two months after knee arthroplasty. *Arthritis & Rheumatism, 47*(5), 484-493. Doi:10.1002/art.10652

Pisetsky, D. S., & McCleane, G. (2009) Pain in Rheumatoid Arthritis and Osteoarthritis. In C. E. Argoff & G. McCleane (Ed.), *Pain management secrets* (3rd ed., pp. 170-183). Philadelphia, PA: Mosby.

Perry, J. (1995). *Gait analysis: normal and pathological function*. (pp. 243). Thorofare, NJ: SLACK.

Petrella, R. J., & Bartha, C. (2000). Home based exercise therapy for older patients with knee osteoarthritis: A randomized clinical trial. *J Rheumatol, 27*(9), 2215-2221.

Piazza, S. J., & Delp, S. L. (1996). The influence on muscles in knee flexion during the swing phase of gait. *Journal of Biomechanics, 29*(6), 723-724. doi: 10.1016/0021-9290(95)00144-1

Quilty, B., Tucker, M., Campbell, R., & Dieppe, P. (2003). Physiotherapy, including quadriceps exercises and patellar taping, for knee osteoarthritis with predominant patello-femoral joint involvement: randomized controlled trial. *J Rheumatol, 30*(6), 1311-1317.

Robon, M. J., Perell, K. L., Fang, M., & Guererro, E. (2000). The relationship between ankle plantar flexor muscle moments and knee compressive forces in subjects with and without pain. *Clin Biomech, 15*(7), 522–527.

Røgind, H., Bibow-Nielsen, B., Jensen, B., Møller, H. C, Frimodt-Møller, H., Bliddal, H. (1998). The effects of a physical training program on patients with osteoarthritis of the knees. *Arch Phys Med Rehabil, 79*(11), 1421-1427.

Salzman, B. (2010). Gait and Balance Disorders in Older Adults. *Am Fam Physician, 82*(1), 61-68.

Sanghi, D., Avasthi, S., Mishra, A., Singh, A., Agarwal, S., & Srivastava, R. N. (2011). Is radiology a determinant of pain, stiffness, and functional disability in knee osteoarthritis? A cross-sectional study. *J Orthop Sci, 16*(6), 719-725. https://doi.org/10.1007/s00776-011-0147-y

Schilke, J. M., Johnson, G. O., Housh, T. J., & O'Dell, J. R. (1996). Effects of muscle-strength training on the functional status of patients with osteoarthritis of the knee joint. *Nurs Res, 45*(2), 68-72

Sellam, J., & Berenbaum, F. (2010). The role of synovitis in pathophysiology and clinical symptoms of osteoarthritis. *Nat Rev Rheumatol*, *6*(11), 625–635.

Sharma, L., Song, J., Felson, D. T., Cahue, S., Shamiyeh, E., & Dunlop, D. D. (2001). the role of knee alignment in disease progression and functional decline in knee osteoarthritis. *JAMA, 286*(2), 188-195.

Sherwood, R. J., & Duren, D. L. (2013). Growth of a species, an association, a science: 80 years of growth and development research. *American journal of physical anthropology*, *150*(1), 1–4. doi:10.1002/ajpa.22178

Shim, H. Y., Park, M., Kim, H. J., Kyung, H. S., & Shin, J. Y. (2018). Physical activity status by pain severity in patients with knee osteoarthritis: a nationwide study in Korea. *BMC musculoskeletal disorders*, *19*(1), 380.

Slemenda, C., Brandt, K. D., Heilman, D. K., Mazzuca, S., Braunstein, E. M., Katz, B. P., & Wolinsky, F. D. (1997). Quadriceps weakness and osteoarthritis of the knee. *Ann Intern Med*, *127*(2), 97– 104.

Studenski, S., Perera, S., Patel, K., Rosano, C., Faulkner, K., Inzitari, M., … Guralnik, J. (2011). Gait Speed and Survival in Older Adults. *JAMA, 305*(1), 50. doi:10.1001/jama.2010.1923

Tan, J., Balci, N., Sepici, V., & Gener, F. A. (1995). Isokinetic and isometric strength in osteoarthrosis of the knee: A comparative study with healthy women. *Am J Phys Med Rehabil*, *74*(5), 364-369.

Teixeira, L. F., & Olney, S. J. (1996). Relationship between alignment and kinematic and kinetic measures of the knee of OA elderly subjects in level walking. *Clin Biomech, 11*(3), 126–134.

Umberger, B. R. (2010). Stance and swing phase costs in human walking. *Journal of The Royal Society Interface*, *7*(50), 1329-1340. doi:10.1098/rsif.2010.0084

van Baar, M. E., Dekker, J., Oostendorp, R. A., Bijl, D., Voorn, T. B., Lemmens, J. A., & Bijlsma, J. W. (1998). The effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: A randomized clinical trial. *J Rheumatol*, *25*(12), 2432-2439.

Vos, T., Allen, C., Arora, M., Barber, R. M., Bhutta, Z. A., Brown, A., ... & Coggeshall, M. (2016). Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet*, *388*(10053), 1545-1602.

Walsh, N. E., & Hurley, M. V. (2009). Evidence based guidelines and current practice for physiotherapy management of knee osteoarthritis. *Musculoskeletal Care*, *7*(1), 45-56.

White, D. K., Niu, J., & Zhang, Y. (2013). Is symptomatic knee osteoarthritis a risk factor for a trajectory of fast decline in gait speed? Results from a longitudinal cohort study

[published correction appears in Arthritis Care Res (Hoboken). 2013 Apr; *65*(4): 666]. *Arthritis Care Res (Hoboken), 65*(2), 187–194. doi:10.1002/acr.21816

Whittle, M. W. (2008). *Gait analysis: An introduction*. (pp. 53, 54, 57, 63). Edinburgh: Butterworth-Heinemann.

Wojdasiewicz, P., Poniatowski, Ł. A., & Szukiewicz, D. (2014). The role of inflammatory and anti-inflammatory cytokines in the pathogenesis of osteoarthritis. *Mediators of inflammation, 2014*, 561459. doi:10.1155/2014/561459

Wong Baker FACES Foundation. (n. d.) *Instructions for Use.* https://wongbakerfaces.org/instructions-use/

Young, A. (1993). Current issues in arthrogenous inhibition. *Annals of the rheumatic diseases, 52*(11), 829–834. doi:10.1136/ard.52.11.829

Zhang, Y., & Jordan, J. M. (2008). Epidemiology of osteoarthritis. *Rheumatic diseases clinics of North America, 34*(3), 515–529. doi:10.1016/j.rdc.2008.05.007

Zhang, W., Moskowitz, R. W., Nuki, G., Abramson, S., Altman, R. D., Arden, N., …Tugwell, P. (2008). OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage, 16*(2), 137-162.

Zhang, S. L., Liu, H. Q., Xu, X. Z., Zhi, J., Geng, J. J., & Chen, J. (2013). Effects of exercise therapy on knee joint function and synovial fluid cytokine levels in patients with knee osteoarthritis. *Molecular medicine reports, 7*(1), 183-186.