THE RELATIONSHIP BETWEEN KNEE PAIN AND BODY WEIGHT IN EARLY ONSET KNEE OSTEOARTHRITIS

BY

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A thesis submitted to the Faculty of Graduate Studies in Partial Fulfillment of the Requirements for the degree of

MASTER OF SCIENCE

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Winnipeg, June 16, 2011
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<td>(ACL)</td>
<td>Anterior Cruciate Ligament</td>
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<td>(AP)</td>
<td>Anterior-Posterior</td>
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<td>(BMI)</td>
<td>Body Mass Index</td>
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<td>(FWB)</td>
<td>Full weight-bearing</td>
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<td>(HR)</td>
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<td>(HTO)</td>
<td>High Tibial Osteotomy</td>
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<td>(Hz)</td>
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<td>(IPA)</td>
<td>Initial Peak Acceleration</td>
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<td>(KOOS)</td>
<td>Knee Osteoarthritis Outcome Score</td>
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<td>(kV)</td>
<td>Kilovolts</td>
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<td>(LBPP)</td>
<td>Lower Body Positive-Pressure</td>
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<td>(mA)</td>
<td>Milliamperes</td>
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<td>(MET)</td>
<td>Metabolic Equivalents</td>
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<td>(ML)</td>
<td>Medial-Lateral</td>
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<td>(MRI)</td>
<td>Magnetic Resonance Imagery</td>
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<td>Non-Steroidal Anti-Inflammatory Drugs</td>
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<td>(PP)</td>
<td>Peak-to-Peak</td>
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<td>(SMA)</td>
<td>Skin Mounted Accelerometer</td>
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<td>(SQUASH)</td>
<td>Short Questionnaire for Assessing Health-Enhancing Physical Activity</td>
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<td><strong>TKA)</strong></td>
<td>Total Knee Arthroplasty</td>
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<td><strong>VAS)</strong></td>
<td>Visual Analog Scale</td>
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ABSTRACT

Osteoarthritis (OA) is a group of diseases entailing degradation of joints, and has been designated as one of the key conditions for special attention during the World Health Organization’s Bone and Joint Decade (2000-2010) (Brooks & Hart, 2000).

Research has demonstrated that body weight is the number one modifiable risk factor associated with the onset and progression of knee OA (Felson, 1996). However, exercise programs that aim to initiate weight loss and improve pain and function in knee OA often increase loading on the knee joint, contributing to degeneration of the knee and progression of the disease (Miyazaki et al, 2002). The introduction of a new anti-gravity treadmill, which utilizes a technology called Lower Body Positive Pressure (LBPP), allows the examination of the relationship between weight, knee pain and knee loading via knee acceleration during exercise. The null hypothesis states that there will be no significant difference in knee pain, knee function and knee joint acceleration when comparing full weight bearing and LBPP treadmill walking exercise in a young knee OA population.

Twenty-two overweight/obese patients with mild or moderate early-onset knee OA were recruited to complete two 25 minute treadmill walking sessions (one full weight-bearing and one LBPP walking session) one week apart and two walkway walking sessions. Knee pain and knee acceleration were recorded. Paired t-tests and ANOVAs were used to compare conditions. On average, an LBPP of 12.3% body weight reduction reduced knee pain in our population. Knee pain was significantly lower during LBPP walking than during full weight-bearing walking. Knee acceleration decreased with increasing LBPP. Heel strike and toe-off data from walkway walking trials illustrated
significantly different knee acceleration about the knee (slow walking loads were lower / fast walking were higher), as compared to treadmill walking sessions. This study illustrates that treadmill walking at a minimal level of LBPP can decrease knee pain and attenuate knee joint loads while allowing patients to complete exercise programs aimed at initiating weight loss and improving pain and function in knee OA. LBPP appears to be a promising tool for rehabilitation for those with painful knee OA and other lower body musculoskeletal conditions.
1. INTRODUCTION

Osteoarthritis (OA) is a group of diseases entailing degradation of joints, and has been designated as one of the key conditions for special attention during the World Health Organization’s Bone and Joint Decade (2000-2010) (Brooks & Hart, 2000). OA can be classified using either symptoms or radiographs (Arden & Nevitt, 2006). Symptomatic OA is characterized primarily by knee pain during most days of the previous month (Arden & Nevitt, 2006), while radiographic OA assesses structural changes such as osteophyte formation and joint space narrowing (Kijowski, Blankenbaker, Stanton, Fine, & De Smet, 2006). Of note is the historically poor correlation between symptomatic and radiographic OA that has been reported (Cicuttini, Baker, Hart, & Spector, 1996; Claessens, Schouten, van den Ouweland, & Valkenburg, 1990). The reason for this poor relationship between symptomatic and radiological OA is unknown. The precise etiology of OA is also unknown, however it is considered by many to be a multi-factorial disease that is attributable to: 1. Systemic factors such as age, gender, hormones, metabolism, genetics, and nutritional factors (Arden & Nevitt, 2006); 2. Mechanical factors including previous joint injury, leg mal-alignment or muscle weakness, and obesity (Reijman, et al., 2007).

Current research focuses on the specific mechanism of action and modification of risk factors, particularly mechanical factors. Previous joint injury appears to greatly increase the risk of early-onset OA (Louboutin, et al., 2009). The role of muscle weakness in the incidence and progression of OA is not clear, although some research indicates a correlation between quadriceps weakness and presence of OA (Segal, et al., 2009); however it is unknown whether quadriceps weakness influences OA development.
or is a result of it. Of the identifiable risk factors, being overweight (BMI >25 kg/m^2) is considered to be the number one modifiable risk factor for the development and progression of knee OA, with one model estimating that approximately a quarter of all cases of total knee arthroplasty for end stage knee OA could be avoided with weight reduction (Coggon, et al., 2001). Research indicates that each one pound of weight loss results in a corresponding 4 pound decrease in knee joint loads during walking (Browning & Kram, 2007; Messier, Gutekunst, Davis, & DeVita, 2005). The effect of weight on knee joint load is thought to be a key variable in the relationship between body weight and knee pain in knee OA (Liikavainio, Bragge, Hakkarainen, Karjalainen, & Arokoski, 2010); however few studies have demonstrated the direct influence of weight on knee joint load. This may be because of study characteristics, such as most research demonstrating only modest weight loss (Christensen, Bartels, Astrup, & Bliddal, 2007; Messier, et al., 2005; Rogers & Wilder, 2008), and contradictory findings on knee joint load in symptomatic knee OA (Liikavainio, et al., 2010; Turcot, et al., 2008). As there are several compounding factors associated with weight loss, (examples: increase in muscle strength, lifestyle changes and dietary modification), the true relationship between weight loss, knee joint load and the impact on knee pain is unknown.

While other treatment strategies focus solely on pain relief or restoring function through surgery, emerging technologies that provide body weight support may isolate the effects of body weight unloading on knee pain in overweight and obese individuals with early onset OA and help in the treatment of this disease. One such device, the G-trainer, uses LBPP to accurately unload an individual to a desired level of body weight (Grabowski & Kram, 2008). This emerging technology was used to assess the effects of
body weight unloading on joint load and knee pain, in an effort to establish a relationship between body weight unloading and knee pain.
2. REVIEW OF THE LITERATURE

2.1 Osteoarthritis

2.1.1 Epidemiology

Osteoarthritis is the most common type of arthritis and a leading cause of disability, making the social and economic cost to the healthcare system vast. Three million Canadians are affected by this chronic disease (Arthritis Society, 2010). The total expense of treating arthritis in the U.S. amounts to $233.5 billion yearly, roughly 10% of the entire U.S. healthcare budget (Bitton, 2009). For osteoarthritis in particular, the cost is approximately $89.1 billion. Approximately 60-70% of older adults display osteoarthritic changes in their knees (Arden & Nevitt, 2006). The burden of disease is also expected to rise in the near future, with estimates of the number of total knee arthroplasties increasing by 673% (Bitton, 2009). With the high cost to the healthcare system, and to the economy from lost time in the labour force, OA has a significant impact on society. Beyond this, the costs increase exponentially when OA affects younger individuals and it is this amplification of dysfunction and disability that is currently being investigated.

2.1.2 Anatomy and Pathology

Osteoarthritis is seen as a wear and tear condition; with all tissues around the knee being affected, most noticeably the cartilage and subchondral bone of the knee. Osteoarthritis is characterized by inflammation, softening, fibrillation, and degradation of articular cartilage, as well as abnormal bone growth in the form of osteophytes (Arden & Nevitt, 2006; Sharma, Kapoor, & Issa, 2006). Other anatomical changes involve the appearance of subchondral cysts, abnormal remodeling of subchondral bone, weakening
of muscles about the knee joint, and joint space narrowing (Arden & Nevitt, 2006; Pearle, Warren, & Rodeo, 2005; Sharma, et al., 2006).

Articular cartilage is an avascular, aneural tissue with low metabolic activity, meant to bear mechanical stresses during loading of a joint (Junqueira & Carneiro, 2005). It receives nutrients from the synovial fluid in the joint through diffusion and has several properties that optimize its load bearing capability, including high shear and tensile strength, and viscoelastic properties including load dissipation and reversible deformation (Pearle, et al., 2005).

Cartilage has two primary components, chondrocytes and an extracellular matrix. Chondrocytes secrete matrix components and maintain the balance between breakdown and regeneration of these components (Junqueira & Carneiro, 2005; Pearle, et al., 2005). The major ingredients of the extracellular matrix are type II collagen, proteoglycans, and water (Pearle, et al., 2005). Type II collagen is the most common form of collagen in hyaline cartilage, and contributes to the solid structure of the extracellular matrix. Its fibers are arranged end to end in the matrix and through cross-linking of fibers, are an important source of shear and tensile strength of cartilage (Pearle, et al., 2005).

Proteoglycans are the key components that resist compression in cartilage by binding to water molecules (Junqueira & Carneiro, 2005). This acts as a shock absorber, with hydraulic pressure allowing cartilage to deform and then return to its original condition (Pearle, et al., 2005). Water is the most abundant component of cartilage, and is bound to the negative charge of the proteoglycan aggregates (Pearle, et al., 2005). This fluid provides several of the viscoelastic properties inherent to cartilage such as its ability to dissipate load, by increasing hydraulic pressure during load-bearing (Pearle, et al., 2005).
While healthy articular cartilage is meant to deform and bear stress during loading (Boocock, McNair, Cicuttini, Stuart, & Sinclair, 2009), osteoarthritic tissue is unable to bear loads in the same fashion and can suffer permanent deformation, resulting in stress that is then transferred to the underlying bone. Because of the loss of shock absorption by articular cartilage, the subchondral bone is forced to bear greater loads that may exceed the yield point of the bone, causing permanent deformation, or even ultimate failure of the tissue (Nordin & Frankel, 2001).

This permanent deformation and degradation of tissue in OA is caused by abnormal mechanical stresses that create an imbalance between extracellular matrix anabolism and catabolism (Brandt, Dieppe, & Radin, 2008). Micro-molecular changes take place, including chondrocyte necrosis, breakdown of proteoglycan architecture, and disorganization of collagen (Pearle, et al., 2005). Loss of chondrocytes results in an inability to repair the matrix and produce extracellular matrix proteins. Breakdown of proteoglycan structure leads to a loss of proteoglycans, and coupled with the disorganization of collagen, accounts for a loss in the strength and load-bearing capabilities of cartilage (Pearle, et al., 2005). While the cartilage initially hypertrophies due to an increase in water, the lack of solid fiber structure in the matrix results in decreased stiffness and strength of cartilage (Pearle, et al., 2005).

The tibiofemoral joint exhibits poor congruence between articulating bones. This joint relies on ligaments, muscles, and fibrous connective tissue structures to increase the stability about the knee and improve the bony fit (Moore, Dalley, & Agur, 2010). Alterations in these stabilizing features – such as ligamentous injury, muscular weakness, biomechanical mal-alignment or anatomical abnormality can lead to increased and abnormal patterns of load bearing and stress inside the knee joint, borne by the hyaline
cartilage. Increased or abnormal mechanical stress can initiate the inflammatory and degradative response of articular cartilage documented on both a macroscopic and microscopic level (Pearle, et al., 2005). It is imperative in the management of this disease to reduce or remove the abnormal and increased mechanical stresses in the joint.

2.1.3 Early-Onset Osteoarthritis

Traditionally, OA is thought to be a disease of the elderly; however in early-onset OA, the signs and symptoms of this debilitating disease appear in middle-aged adults (Gelber, et al., 2000; Golightly, Marshall, Callahan, & Guskiewicz, 2009; Lohmander, Englund, Dahl, & Roos, 2007). The age of early onset can be 10-20 years earlier than the average age of onset of the disease (Gelber, et al., 2000). There are several factors that may specifically increase the risk of early-onset OA. Research examining the relationship between knee joint injuries and OA onset has illustrated that degenerative joint changes are evident “in approximately every other knee”, at ages where OA is uncommon in the population (Roos, 2005). Individuals who suffer ACL or meniscus tears are more likely to develop OA than those in the general population, with a prevalence rate of early-onset knee OA of 50-100% 10-20 years after initial injury (Gelber, et al., 2000; Golightly, et al., 2009; Lohmander, et al., 2007; Louboutin, et al., 2009). Placed in context, this means that a person that suffers a knee joint injury in their late teens or early twenties is at increased risk for the development of knee OA while still in their 30’s or 40’s, at a time in life when their physical demands and expectations are still very high, both at work and during recreation participation (Roos, 2005). As one author describes, the rate of radiographic knee OA in this “young patient with an old knee” population is on par with
that of uninjured individuals at about 70 years of age (Lohmander, et al., 2007; Roos, 2005).

2.2 Classification & Symptomology

The classification of knee OA can be undertaken using two different methods: radiography or symptomology. Classification according to radiographic criteria aims to assess structural changes in the joint relating to the disease, and is widely used in epidemiological studies. However, OA can also be classified according to symptomology, and this method is often used in clinical settings. The correlation between symptoms and radiographic evidence of OA appears to be poor (Cicuttini, et al., 1996; Claessens, et al., 1990; Paradowski, Englund, Lohmander, & Roos, 2005). Patients may exhibit advanced levels of OA on radiograph but be asymptomatic, while some patients suffer severe symptoms with little evidence of joint degradation. Some studies have shown a stronger correlation between OA and specific features on radiograph, such as osteophytes (Arden & Nevitt, 2006; Felson, et al., 1997). Further, radiographic grading of OA seems to be most accurate in more advanced stages of OA (stage 2 or greater), when compared to arthroscopy or symptomatic OA (Felson, et al., 1997; Kijowski, et al., 2006). Recently, Neogi et al (2009) has shown a strong correlation between radiographic severity of OA and knee pain, using patients with knees that exhibited discordant levels of pain. This method appears to remove the confound of comparing between patients, and may for this reason more clearly highlight the relationship between structural and symptomatic OA. Recently, symptomatic OA has been defined as the presence of both radiographic OA and symptoms (Segal, et al., 2010). However, use of this definition may exclude patients with either radiographic changes or symptoms alone who may still benefit from treatment.
OA can be divided into primary, considered idiopathic, and secondary, OA (Arden & Nevitt, 2006). Secondary OA results from a previous condition, and can be subdivided into metabolic (i.e. Acromegaly), anatomic (i.e. slipped femoral epiphysis), traumatic (i.e. joint injury or surgery), or inflammatory (i.e. septic arthritis) categories (Arden & Nevitt, 2006). OA may also be further classified according to certain features, such as erosion (erosive arthritis) or OA with chondrocalcinosis (Arden & Nevitt, 2006). The appearance of OA in different joints is also of note, with a significant correlation between the development of hand and knee OA (Arden & Nevitt, 2006).

2.2.1 Symptomatic OA

Clinically, knee OA is primarily characterized by progressive joint pain and stiffness (Arden & Nevitt, 2006; Jinks, Jordan, & Croft, 2007; Sharma, et al., 2006). Clinical OA is diagnosed according to the definition developed by the American College of Rheumatology, which uses joint pain on most days of the prior month as the major inclusion criteria (Arden & Nevitt, 2006). Other symptoms evident in OA include decreased range of motion about the knee, tenderness, crepitus, swelling and progressive inflammation (Arden & Nevitt, 2006; Sharma, et al., 2006). These symptoms, especially knee pain, have been shown to initiate a decrease in physical function, such as the ability to perform normal activities of daily living such as walking, squatting or kneeling (Jinks, et al., 2007). Research examining the relationship between knee pain and physical activity levels in a knee OA population has demonstrated that these parameters are highly correlated, with the onset and severity of knee pain being closely linked to functional declines in a knee OA population (Jinks, et al., 2007). The resulting lifestyle modifications can lead to an overall sedentary lifestyle that manifests as a decrease in
overall physical conditioning and an increase in body weight. These changes can further negatively impact the knee joint, and a negative cycle of joint degradation leading to lifestyle modification and further degradation begins.

2.2.2 Radiographic OA

Knee OA is most commonly diagnosed using radiography. This aims to assess the structural changes inherent to OA, including the presence of osteophytes, joint space narrowing, subchondral sclerosis, cyst formation, and bony contour changes (Arden & Nevitt, 2006; Felson, et al., 1997; Kellgren & Lawrence, 1957; Sharma, et al., 2006). There are many radiographic criteria that exist, including the Kellgren & Lawrence, Ahlback, and Brandt OA grading scales (Kijowski, et al., 2006). The most frequently used grading scale is the Empire Rheumatism Council scale by Kellgren and Lawrence (Arden & Nevitt, 2006; Felson, et al., 1997; Kellgren & Lawrence, 1957; Sharma, et al., 2006). This scale follows a progression from 0 (indicating no signs of OA) to 4 (severe structural OA changes present), with the use of progressive joint space narrowing, osteophyte appearance, bone sclerosis and cyst appearance as criteria (Arden & Nevitt, 2006; Kellgren & Lawrence, 1957). This scale has been validated against arthroscopy (Kijowski, et al., 2006), and is reproducible and reliable (Arden & Nevitt, 2006). However, some studies have shown that radiographic grading scales, and in particular the Kellgren-Lawrence scale, is not very sensitive in assessing early-stage disease (Kijowski, et al., 2006).
2.2.3 Magnetic Resonance Imaging (MRI)

MRI can also be used to assess structural changes in OA. While radiographs are still considered the gold standard when assessing structural change in OA, the popularity of MRI for imaging knee OA is growing (Guermazi, et al., 2003). Reasons for this may include the fact that MRI does not emit harmful radiation, can provide multiplanar views of soft tissue structures about the knee joint, and can be used to visualize tissue in detail (Bureau, Kaplan, & Dussault, 1995; Guermazi, et al., 2003). In radiography, joint space narrowing is used to estimate articular cartilage loss. By contrast, MRI provides clear images of articular cartilage, menisci, subcortical bone marrow, muscles and ligaments, and can quantify chronic changes in cartilage and menisci (Guermazi, et al., 2003).

Features of osteoarthritic knees on MRI include cartilage defects and cartilage thinning, osteophyte formation, subchondral bone marrow edema, subarticular cysts, subchondral sclerosis, bone attrition, meniscal maceration, joint effusion, loose bodies, and ligamentous abnormalities (Bureau, et al., 1995; Guermazi, et al., 2003; Manaster, Johnson, & Narahari, 2005). In particular, preliminary studies have shown a correlation between knee pain and meniscal maceration (Guermazi, et al., 2003). This method may help to clarify the relationship between structural changes in OA and symptoms. Several different pulse sequences and features in the grading of OA have been suggested (Bureau, et al., 1995), but currently a standardized classification criteria or method of imaging has not been developed. For this reason, radiography is still more commonly used, especially in large epidemiological studies (Messier, et al., 2004; Neogi, et al., 2009; Segal, et al., 2010).
2.3 Risk Factors

No single cause of OA has been elucidated. However, there are many factors that appear to increase the risk of OA and correlate with the incidence or progression of OA. Risk factors can be broadly divided into two categories: systemic and mechanical factors (Arden & Nevitt, 2006).

Systemic factors both directly and indirectly affect joint deterioration. Increasing age, female gender, and estrogen deficiency may indirectly increase the risk of OA (Arden & Nevitt, 2006; Sharma, et al., 2006). Racial differences in OA have also been shown, with African American patients displaying higher levels of pain and disability for each radiographic grade of OA (Sims, et al., 2009). Further, a multitude of genes and high bone density may increase susceptibility to OA, while intake of antioxidants may decrease the oxidative stress on cartilage and ensuing damage (Arden & Nevitt, 2006). Anatomic features such as cartilage volume and medial chondral defects have a strong heritability component (Sharma, et al., 2006). The role of leptin in OA is currently being investigated, with studies showing increased levels of the hormone in the synovial fluid of osteoarthritic joints (Dumond, et al., 2003; Ku, et al., 2009; Lago, Gomez, Lago, Gomez-Reino, & Gualillo, 2008). Leptin appears to play a role in inflammatory function, suggesting a role in the inflammatory process in OA (Lago, et al., 2008). The progression of OA has also been linked to the incidence of atheromatous vascular disease (Conaghan, Vanharanta, & Dieppe, 2005).

There are several mechanical factors that can increase the risk of OA, including leg alignment, proprioception, muscle weakness, obesity, previous joint injury and surgery (Arden & Nevitt, 2006; Blagojevic, Jinks, Jeffery, & Jordan, 2010; Sharma, et al., 2006). Of particular interest is obesity, as it is the number one modifiable risk factor in
OA. Recent research has looked at the effect of body weight on knee pain, knee OA incidence and progression. Obesity has been shown to be positively correlated with proteoglycan metabolism (Buchholz, et al., 2010). This increase in metabolism is similar to cartilage responses to compression and may signify the initial, inflammatory stages of OA.

2.3.1 Leg Alignment and Proprioception

Varus alignment (where knees angle laterally, creating lower extremity bow-leggedness) has been shown to increase the risk of medial compartment OA, while valgus alignment (where knees angle medially, creating lower extremity knock-knees) may slightly increase the risk of lateral compartment OA (Niu, et al., 2009). Obesity seems to further heighten this risk in valgus knees, however not in varus knees (Niu, et al., 2009). It is thought that perhaps varus alignment alone may be a strong enough mechanical stressor to initiate OA development. Patients with knee osteoarthritis, especially those with varus alignment, are also more likely to have a heel strike transient and a sharp peak in the initial ground reaction force curve, which may increase mechanical stress on the knee joint (Hunt, et al., 2010). Poor joint proprioception has also been associated with knee OA, however this correlation was seen only in cross-sectional, and not longitudinal, studies (Segal, et al., 2010). In one particular study, joint proprioception in a non-weight bearing position was assessed, and this was not associated with development of knee OA over a 30 month period (Segal, et al., 2010). Proprioception is correlated with knee joint pain, and so it may be that non-weight bearing assessment allows the bias of knee pain to be removed. However, assessment of proprioception in a static, non-weight bearing setting may not accurately reflect a patient’s functional proprioception. Further,
quadriceps strength is known to be correlated with the incidence of knee OA, and weight bearing tests of proprioception that have shown a correlation between joint position sense and knee OA may rely more on muscular input and the relationship between strength and OA (Segal, et al., 2010).

2.3.2 Muscle Strength

The evidence describing the relationship between OA and muscle strength is contradictory. Some studies have found an association between symptomatic OA (but not radiological OA) and decreased knee extensor strength, with a particular effect on knee pain (Focht, Ewing, Gauvin, & Rejeski, 2002; Segal, et al., 2009; A. C. Thomas, Sowers, Karvonen-Gutierrez, & Palmieri-Smith, 2010). More specifically, quadriceps strength has been correlated with incidental symptomatic OA (Roos, 2005; Segal, et al., 2009). Differences in findings may be attributed to how strength is analyzed, with differing methods of comparing strength to body weight, BMI and BMI on a logistic scale (Segal, et al., 2009). While weak quadriceps strength OA patients has been associated with attenuated joint loads, new research suggests that this may be confounded by walking speed. OA patients with weak quadriceps strength were found to voluntarily choose lower walking speeds resulting in lower joint loads experienced (Hunt, et al., 2010). However in the above study, quadriceps strength was measured by a maximal isometric contraction at 60° of knee flexion (Hunt, et al., 2010), and this may not reflect quadriceps function during walking. Further, strength of other muscles, such as hip abductors and hamstrings, which are also thought to play a role in knee joint loading, were not assessed. Improvements in quadriceps strength have been shown to improve OA symptoms among
patients (Jenkinson, et al., 2009; Messier, et al., 2004), however most studies that assess exercise interventions on OA are confounded by concomitant weight loss. For this reason, it may be difficult to attribute improvement to strengthening, weight loss, or lifestyle changes solely, or to some combination of the above. Further, optimal exercise prescription in knee OA patients has not been determined, with only one study showing similar results of improvement in pain and physical function between a walking program and a home based quadriceps strengthening program (Evcik & Sonel, 2002).

2.3.3 Previous Injury

An influential risk factor for OA, and importantly, the development of early-onset OA, is previous traumatic injury to the knee joint. The increased risk of OA development after injury varies widely within the literature. One prospective cohort analysis found a doubling in the risk of OA development to 14% for medical students that sustained a traumatic knee injury (Gelber, et al., 2000). Professional athletes that often suffer from multiple traumatic injuries throughout their career were found to have much higher levels of OA, up to 43% (Golightly, et al., 2009), although this figure was based on all professional football players surveyed, and not just those that may have suffered a traumatic knee injury. This may suggest that the incidence among those suffering traumatic knee injuries is even higher. Von Porat, Roos & Roos (2004) reported radiographic OA equivalent to Kellgren-Lawrence grade II or higher in 40% of soccer players that had previously suffered from an anterior cruciate ligament (ACL) tear. Traumatic injuries, such as ACL tears or meniscal lesions, can disrupt the mechanics of the knee joint and over time contribute to the wear and tear of the joint (Roos, 2005).
There may be several reasons for the increased risk of OA. After the occurrence of an injury, such as the tearing of the ACL, the shear forces on the joint, and specifically the articular cartilage, are increased (Louboutin, et al., 2009). Further, inflammatory markers are released at the time of injury, and this may disrupt the homeostasis of extracellular matrix-producing chondrocytes (Louboutin, et al., 2009). Meniscal tears strongly correlate with OA development, with degenerative meniscal tears showing a poorer prognosis when compared to traumatic tears (Englund, Roos, & Lohmander, 2003). Chondral lesions may also occur at the time of injury, and the low metabolic rate of chondrocytes may not allow adequate repair of such defects, increasing the risk of further degenerative changes and ultimately, OA of the knee (Louboutin, et al., 2009).

Injury to the structures about the knee can be traumatic at the time of injury, but can also disrupt the mechanics of the knee after injury. Knee adduction moment, a variable often increased in osteoarthritic patients as compared to normals, is also found to be greater in individuals who have suffered from an ACL tear and subsequent repair (Butler, Minick, Ferber, & Underwood, 2009). This seems to indicate a progression towards gait patterns more commonly seen in OA patients.

2.3.4 Surgery

After a traumatic knee injury, surgical repair of damaged structures is often attempted. Trauma incurred during surgery may also increase the risk of knee OA, similar to trauma incurred during injury. Certain surgeries have been associated with an increased risk of early OA development, specifically menisectomies. The risk of OA development for individuals that have had menisectomies varies widely, with studies showing 50-100% development of OA in menisectomy patients (Lohmander, et al., 2007;
of OA development (Lohmander, et al., 2007; Louboutin, et al., 2009; Roos, 2005). Indeed, some studies suggest an improved outcome for conservatively managed ACL tears, although the rate of OA development among these patients is still high at 15% (Neuman, et al., 2008). There may be many reasons for the lack of evidence for ACL repair, such as poor or variable ACL repair techniques, other factors in the pathological process driving the degeneration, and methodologically poor clinical studies (Lohmander, et al., 2007). Other factors may also confound the ACL repair and risk of OA relationship, such as meniscal lesions that may be sustained during ACL rupture and subsequent menisectomies that may be performed concurrently, as well as differences in activity level of patients with surgically and non-surgically repaired ACL tears (Neuman, et al., 2008). Importantly, individuals that suffer from traumatic knee injury and subsequent surgery tend to develop OA at a much younger age as compared to the general population, with the onset of OA between 30-50 years of age (Gelber, et al., 2000; Lohmander, et al., 2007; von Porat, et al., 2004). The average age of OA onset in the general population is approximately 57 years of age (Gelber, et al., 2000), and this represents a significant difference in age at onset, identifying early-onset OA individuals as the young patient with the old knee (Lohmander, et al., 2007). Preventing and treating OA is paramount in this population, to decrease the risk of OA after injury and surgery.

2.3.5 Obesity

Of the identified risk factors, obesity, specifically BMI (Lohmander, Gerhardsson de Verdier, Rollof, Nilsson, & Engstrom, 2009) is believed to be the number one modifiable risk factor for the development and progression of knee OA. An increased
BMI increases the risk of knee pain among patients that display radiographic signs of OA (Rogers & Wilder, 2008). Further, obesity is associated with both symptomatic and radiographic knee OA (Niu, et al., 2009; Paradowski, et al., 2005; Reijman, et al., 2007). However, the results on obesity influencing progression of this disease are contradictory (Niu, et al., 2009; Reijman, et al., 2007). It is thought that perhaps confounding factors, such as leg alignment, may be responsible for the different results, as varus alignment is a powerful predictor of knee OA progression in itself (Niu, et al., 2009). However the influence of excess weight on joint degradation has clearly been demonstrated. It is correlated with bilateral OA and can increase the risk of OA four-fold (Felson, 1996a, 1996b).

There is a significant alteration of gait and joint load in obese individuals, and evidence suggests that osteoarthritic changes may partly be due to abnormal biomechanics resulting from obesity (Powell, Teichtahl, Wluka, & Cicuttini, 2005). Recent research has shown that ground reaction forces increase proportionately with weight (Messier, et al., 2005), and obese individuals demonstrate longer time spent in stance phase, indicating a longer portion of time spent loading the joint (Browning & Kram, 2007). Muscle moments, specifically hip and knee extensor moments, are also greater in obese individuals, indicating more work performed by the muscles to maintain the proper walking kinematics; however these differences disappear once researchers control for weight (Browning & Kram, 2007). When one considers that a force of roughly three to six times body weight is exerted across the knee joint during single stance in walking, it is clear that an increase in body weight may lead to excessive load, resulting in a corresponding increase in joint related pain across the knee when an overweight person walks (Felson, 1996a, 1996b; Niu, et al., 2009).
Research is conflicting about the relationship between weight loss and knee pain, with some research showing improvements in pain while others show only improvements in function (Christensen, Astrup, & Bliddal, 2005; Jenkinson, et al., 2009; Messier, et al., 2005). Messier et al (2000) found no improvement in pain and function when comparing a weight loss and exercise group of knee OA patients to an exercise alone group of OA patients. However recent research examining the relationship between weight loss and function in an overweight knee OA population illustrates that an average weight loss of 5% of body weight over an 18 month period results in a 24% improvement in function and significantly diminishes knee joint pain (Messier, et al., 2005; Messier, et al., 2004; Rogers & Wilder, 2008). The accuracy of applying this model to larger amounts of weight loss is unknown, as the weight loss recorded by Messier et al (2005) was mild, with an average loss of 2.4 kg, a reduction of only 2.6 % of body weight. Weight loss is difficult to initiate in overweight and obese populations, and even more so in those with pathological conditions, with the most effective approach to date seen in studies that employ low-energy diets. Christensen et al (2005) reduced food intake by 32% (from 5 MJ to 3.4MJ/day) using a high protein nutrition powder for a resultant average weight loss of 11% body weight in 8 weeks. However most weight loss studies, especially those that target patients with knee pain, suffer from high attrition rates (about 10 – 20%) (Christensen, et al., 2005; Jenkinson, et al., 2009; Messier, et al., 2004). Weight loss is believed to significantly influence the risk of developing symptomatic knee OA in obese patients, and weight loss and regular exercise are recommended treatment strategies by both the American College of Rheumatology, and the European League Against Rheumatism (Browning & Kram, 2007). Unfortunately, research to date has been unsuccessful at determining the amount of weight loss needed to alleviate symptoms and
prevent disease progression in a knee OA population (Christensen, et al., 2007; Felson, 1996b). Most studies demonstrate only modest weight loss among patients (Messier, et al., 2005). A reduction of greater than 5% of body weight is recommended (Christensen, et al., 2007); however few studies have demonstrated such levels of weight loss (Christensen, et al., 2005).

The largest amount of weight loss results from patients that undergo bariatric surgery. While not all bariatric surgery patients have knee OA, most exhibit considerable joint pain. After this procedure, patients lose on average 44 kg, with a resulting diminishment or altogether disappearance of knee pain (Lementowski & Zelicof, 2008). This indicates that larger amounts of weight loss may better illuminate the relationship between weight loss and knee pain that is often hidden in more modest amounts of weight loss. Weight loss itself is a complex process that often includes several changes made by the patient over time. Weight loss may be a result of a change in diet, initiation of an exercise program, other lifestyle changes or a combination of the above. Therefore, weight loss can be accompanied by a number of other variables, for instance changes in muscle strength, body composition, and aerobic fitness. Indeed, many studies employ a combination of dietary change and exercise to bring about the change in weight, as well as counseling and behavioural therapy for patients (Christensen, et al., 2005; Jenkinson, et al., 2009; Messier, et al., 2004). This multifaceted approach, while effective, makes it difficult to isolate the relationship between weight and knee pain.

2.3.4 Knee Joint Biomechanics during Ambulation

Gait analysis is often undertaken to assess walking patterns and the loads on the weight-bearing joints of the body. Gait can largely be broken down into four parts, three
of which are weight-bearing: heel strike, mid-stance, and toe off; and one of which is non-weight bearing: swing (Nordin & Frankel, 2001). During heel strike, the quadriceps eccentrically contracts to absorb force in the transition from heel strike to mid-stance, as the extended knee flexes (Nordin & Frankel, 2001). Muscles stabilize during mid-stance; during toe off, there is a large burst of muscle activity in the gastrocnemius to generate force, by ankle plantar-flexion, for push off (Nordin & Frankel, 2001). Finally, during the first part of swing the dorsiflexors and hip flexors are active to allow the foot to clear the ground, before the hamstrings contract eccentrically to decelerate the limb for heel strike (Nordin & Frankel, 2001). Large reference studies have been done on healthy subjects to better understand gait mechanics and the loads on the knee joint during walking. Auvinet et al (2002) showed that healthy subjects walked with a symmetrical gait, with men having longer strides and walking with higher speeds than women. Studies on healthy subjects have shown a significant and strong relationship between walking speed and knee acceleration (Voloshin, 2000). Healthy adults also tend to walk with more extended knees and hips, which may help absorb impacts during weight-bearing (Henriksen, et al., 2006), and they tend to spend a minimal amount of time in double support (with both feet on the ground). With age, both genders show a decrease in walking speed, starting around the sixth decade of life (Auvinet, et al., 2002; Chen, et al., 2003). Further, younger adults normally exhibit a robust gait with two force peaks during weight-bearing; one of these peaks is normally lost with age (Chen, et al., 2003). These studies show a general trend toward gait alterations that reduce knee loading with age: a slower walking speed (indicative of lower knee acceleration), and the loss of force peaks during weight-bearing.

Knee load can be artificially altered through surgery. High tibial osteotomies (HTO) alter knee alignment to try to reduce the loading on a specific compartment of the
knee. For those with varus alignment, this procedure has been shown to reduce the knee adduction moment and medial loading of the knee joint (Lind, et al., 2011). HTO has also been shown to be effective in those with medial knee OA at reducing symptoms and progression of the disease; however this surgery is only a temporary solution, with one study showing the length of survival of the surgery (until knee replacement or another procedure is completed) being just beyond 5 years (Sterett, Steadman, Huang, Matheny, & Briggs, 2010).

Recent research has found several associations between OA and alterations in gait parameters. However, it is unknown whether gait changes occur as a result of joint degradation from disease, or whether abnormal gait patterns result in the degenerative changes witnessed in OA.

Patients with OA, even in early stages, have been shown to have significantly greater external adduction moments when compared to normal controls, a proxy for medial knee joint loads (Baliunas, Ryals, Hurwitz, Karrar, & Andriacchi, 2000) and OA patients walk with more flexed knees and hips, which limits their ability to absorb loads during walking (Henriksen, et al., 2006). There may also be a relationship between an increase in the external adduction moment at the knee, which places an increased load and stress on the medial compartment of the knee and medial meniscus, and knee pain (Amin, et al., 2004). Globally, those with knee osteoarthritis tend to have slower strides than similar-aged healthy controls, resulting in a slower walking speed, and spend longer time in double support (Chen, et al., 2003; Hunt, et al., 2010). Ground reaction forces and vertical tibial accelerations have been found to be significantly lower in patients with painful knee OA (Chen, et al., 2003; Kaufman, Hughes, Morrey, Morrey, & An, 2001; Liikavainio, et al., 2010). This may represent biomechanical modifications (slowing gait,
reducing ground reaction forces and accelerations, and trying to disperse load among both feet) adopted by patients to help reduce stress on the knee joint. Further, knee pain appears to initiate a protective pain reflex (Henriksen, Graven-Nielsen, Aaboe, Andriacchi, & Bliddal, 2010; Schnitzer, Popovich, Andersson, & Andriacchi, 1993; Shrader, Draganich, Pottenger, & Piotrowski, 2004) where patients with painful knee OA tend to adopt gait alteration patterns to attenuate joint loading and acceleration. Henriksen et al. (2008) looked at temporary pain, made to mimic knee OA pain by saline injection, in healthy volunteers and the effect on gait variables; a decrease in acceleration was seen with pain, although the trend was not significant, due in part to the location of saline injection. Beyond this, pain relief appears to reverse this protective pain reflex. Knee OA patients that were given NSAIDs for four weeks exhibited increased knee loading during gait including increased knee adduction moments (Schnitzer, et al., 1993). This may have an important implication for the treatment of OA, as treatments that focus solely on pain relief may actually be inadvertently damaging to cartilage and other knee joint structures.

New research suggests a complex relationship between BMI, OA and gait (Nebel, et al., 2009). Peak vertical force is one gait parameter that has been examined. One study has shown that variations in peak vertical force during gait in knee OA patients can be explained by BMI, self-reported physical function and radiographic grade of knee OA (Nebel, et al., 2009). At fast walking speeds, self-reported physical function accounted for the greatest amount of variation. Self-reported pain was not a strong predictor of variation in peak vertical force, and overall the measured parameters only accounted for 20-30% of the variation present (Nebel, et al., 2009), thus there may be other variables that better explain peak vertical force variation. Other biomechanical variables, such as linear acceleration, were not assessed by Nebel et al. (2009). There are contradictory
findings on linear acceleration, thought to represent instability and shear forces in the knee joint, in OA and healthy controls, with some studies showing significant differences in the medial-lateral and anterior-posterior planes (Turcot, et al., 2008, 2009); while other studies show no differences between groups during walking (Liikavainio, et al., 2010). This may be because of differences in average BMI of the patient population observed between studies, with Turcot et al. (2008) demonstrating a much higher BMI in the OA group. While both studies documented knee pain in the OA population, only Liikavainio et al. (2010) measured the severity of knee pain using a VAS, and for this reason, the difference in pain between studies is unknown and may contribute to the variation in the results. Differences between femoral and tibial vertical acceleration, thought to represent the load transmission ability of a patient, are smaller in those with knee OA, as acceleration is poorly attenuated at the knee (Turcot, et al., 2009). Further, medial-lateral and anterior-posterior accelerations tend to be higher in those with knee OA than healthy controls (Turcot, et al., 2009). This is similar to patients who have suffered ACL tears (Yoshimura, Naito, & Zhang, 2002) and may represent directional instability in the joint. Differences in gait are also highlighted in more demanding tasks such as stair climbing, where greater accelerations about the knee, indicative of greater shear force, are apparent in knee OA patients (Liikavainio, et al., 2010).

2.4 Treatment

Because OA is an incurable joint disease, non-operative treatment strategies focus on optimizing the patient’s quality of life through the reduction of joint pain and enhancement of their functional capacity (Evcik & Sonel, 2002). Treatment strategies include weight loss, pharmacologic intervention, exercise, and ultimately, surgery.
Research has also been carried out on preventative measures, in an effort to circumvent unnecessary pain, suffering, and healthcare costs.

2.4.1 Prevention

Research into the prevention of OA has focused primarily on modifying or eliminating risk factors of the disease. Weight loss has been suggested as a primary strategy to prevent or slow the progression of OA, with one study estimating the avoidance of a quarter of all total knee replacement cases for end-stage knee OA if weight loss to within normal BMI ranges (18.5 – 24.9) were to be obtained (Coggon, et al., 2001). However a clear relationship between weight loss and function or symptomatic improvement has not been derived (Christensen, et al., 2007). A concurrent strategy that has been suggested is educating individuals and patients about the disease, modifiable risk factors, and lifestyle changes to minimize their risk (Jordan, et al., 2003; A. Thomas, et al., 2009). While this suggestion has been made, specifically to target high risk groups (Coggon, et al., 2001), there has been little research done on the success of implementing such programs. This approach is often used as a control case in studies (Jenkinson, et al., 2009; Messier, et al., 2005). Extensive rehabilitation after injury has also been cited as lowering the risk of OA (Neuman, et al., 2008), however injury treatment has not been standardized, and currently there is no optimal treatment to minimize the risk of early-onset OA. If possible, the avoidance of high risk activities has also been suggested, including sports with a high risk of injury and surgical procedures that amplify the risk of OA, such as menisectomies (Roos, 2005; Shephard, 2003). Surgery may not be avoidable at all times, and with growing levels of obesity in the developed world, sport avoidance in particular may not be favorable.
2.4.2 Pharmacologic Intervention

Pharmacologic intervention is one of the most popular forms of treatment in OA. It is primarily used to alleviate symptoms, and has been proven to be effective (Jordan, et al., 2003). However some pharmacologic agents, such as NSAIDs, may increase the risk of gastrointestinal ulcers (Jordan, et al., 2003). Corticosteroids and hyaluronic acid have also been recommended for temporary relief of symptoms. Corticosteroids decrease inflammation while hyaluronic acid aims to increase synovial fluid viscosity to improve shock absorption and articular cartilage protection (Bannuru, et al., 2009). Hyaluronic acid has been found to be effective for longer periods, while corticosteroids were most beneficial in the initial 4 weeks of treatment (Bannuru, et al., 2009). However, pain relieving treatments alone may actually increase loads in the knee joint, further contributing to the degenerative process (Schnitzer, et al., 1993; Shrader, et al., 2004). The combination of pain relieving treatments as well as treatments aimed at moderating knee joint load may be advisable to offset loading increases seen with pain relief. Importantly, gait parameters are responsive to treatment, and while specific treatments to reduce knee loading and acceleration are unclear, some success has been achieved with muscle strengthening, gait retraining, and the use of wedged insoles (Ogata, Yasunaga, & Nomiyama, 1997; Turcot, et al., 2009).

2.4.3 Exercise

Exercise has been frequently suggested as a treatment to reduce symptoms in OA. Muscle strength has been linked to reduced symptoms and OA severity, although the direction of the correlation is unclear (Segal, et al., 2009; A. C. Thomas, et al., 2010).
Exercise has often been prescribed as a program (Messier, et al., 2004); individual elements of exercise prescription, such as range of motion or muscular endurance, have not been isolated and their efficacy alone is not known. The current literature supports the notion that aerobic and lower body resistance exercise can improve patient physical function and decrease knee pain (Jenkinson, et al., 2009; Jordan, et al., 2003; Messier, et al., 2004). One study found stretching and resistance exercises of the quadriceps improved WOMAC pain and physical function scores (Jenkinson, et al., 2009).

Resistance exercises prescribed are often isometric or controlled isotonic knee extension exercises, open chain quadriceps, hamstrings, and calf exercises (Jenkinson, et al., 2009; Messier, et al., 2004).

Aerobic exercise, often prescribed as a walking program, has also been found to be effective in reducing knee pain in OA (Jenkinson, et al., 2009; Jordan, et al., 2003). Jenkinson et al. (2009) combined range-of-motion, resistance and aerobic exercise to produce beneficial effects for OA patients, and so the effects of each cannot be distinguished. The benefit of exercise seems to be additive when exercise and nutritional intervention are combined to produce weight loss (Jenkinson, et al., 2009; Messier, et al., 2004).

Work group recommendations from the 2002 Exercise and Physical Activity Conference (St. Louis, MI) specifically recommend 30 minutes of moderate intensity aerobic exercise, 50-70% of maximal heart rate, on 3 or more days of the week for those with knee OA (Minor, 2003). A general lower body exercise program is also recommended, with the goal of improving strength, endurance, coordination, balance, and function (Minor, 2003). In both recommendations, creating individual-specific exercise programs is advocated. Exercise-adherence is often problematic, and class-based
programs appear to improve adherence, as well as elicit further pain reduction in patients over home based exercise programs (A. Thomas, et al., 2009). Supervision of proper technique and intensity of exercise may contribute to this difference. Exercise may also be prescribed in different mediums, and aquatic exercise or hydrotherapy is recommended, with no differences found in improvement between land and water based programs (Jordan, et al., 2003; A. Thomas, et al., 2009). Exercise has been found to induce a transient increase in pain (Focht, et al., 2002), and the mechanism behind this is unknown; however it is speculated that non-weight bearing or lower impact activities may reduce this pain. Patients that experience less pain may adhere to exercise programs better.

2.4.4 Body Weight Support

Body weight support is an emerging technology in the rehabilitation of lower body injuries. Body weight support aims to reduce the load on joints to allow the re-learning or rehabilitation of ambulation in a graded fashion (Norman, Pepin, Ladouceur, & Barbeau, 1995; Quigley, et al., 2000). Body weight support may also aid research in clarifying relationships between variables including body weight, gait and knee pain in knee OA.

Body weight support has been effectively used as a method of rehabilitation in stroke patients and individuals with neuromuscular disease or disorder, including Down syndrome, Cerebral Palsy, and spinal cord injury (Damiano & DeJong, 2009; Norman, et al., 1995). The use of this method in the rehabilitation and research of lower body injuries is in its infancy, with the possibility of using this technology for lower body fractures, OA, and obesity; however few studies have been done (Mangione, Axen, & Haas, 1996).
The use of LBPP aims to reduce loads on the lower body similar to the effect of individuals losing weight – however this assumption has not been tested and it is unknown if LBPP creates the same alterations in biomechanics and joint forces that losing weight would. Earlier methods of body weight support often utilized a harness system (Colby, Kirkendall, & Bruzga, 1999; Norman, et al., 1995; Teunissen, Grabowski, & Kram, 2007) or water immersion (Wyatt, Milam, Manske, & Deere, 2001). However, there are several disadvantages to these systems. Harness based systems may disrupt the biomechanics of ambulation because of the restrictive harness around the hips, which is particularly important for patients who may be re-learning the neuromuscular patterns of walking (Norman, et al., 1995; Ruckstuhl, Kho, Weed, Wilkinson, & Hargens, 2009; Teunissen, et al., 2007; E. E. Thomas, De Vito, & Macaluso, 2007). Harnesses may affect the economy of running by placing a slight forward force through the harness on the individual, instead of providing an overall vertical unloading force at the person’s centre of gravity (Teunissen, et al., 2007). Harnesses may also cause discomfort by rubbing or pinching during motion. Other systems used for unloading during rehabilitation, such as water based systems tend to be expensive, and require a pool (Mangione, et al., 1996; Quigley, et al., 2000). Further, the muscle contraction occurring in water may not accurately reflect that which occurs on land, and thus may be a poor medium for patients to re-learn the proper biomechanics of ambulation (Cutuk, et al., 2006; Quigley, et al., 2000).

In an effort to provide a more biomechanically realistic as well as accessible form of treatment, a treadmill-based LBPP system was developed (Quigley, et al., 2000). LBPP is a new technology that allows unloading of the lower extremities during exercise in a pressurized treadmill chamber (Figure 1), with lower percentages of body weight
unloading indicating less support. This device utilizes a treadmill contained in a waist-
high air tight chamber, and small increases in chamber air pressure to produce LBPP
which creates a lifting force approximately at the person’s centre of mass (Eastlack, et al.,
2005; Grabowski & Kram, 2008). Air pressure inside the chamber can be easily adjusted
to provide a lifting force that is capable of supporting up to 80% of a subject’s body
weight, offering the ability to accurately and reliably titrate weight bearing loads with
small pressure adjustments within the chamber (Cutuk, et al., 2006). Research has
demonstrated that LBPP can be used to significantly reduce ground reaction forces at the
knee joint, while maintaining normal patterns of muscle activation, joint motion, limb
swing mechanics and cardiovascular function during walking (Colby, et al., 1999; Cutuk,
et al., 2006; Eastlack, et al., 2005; Hargens, Cutuk, White, Rabbani, & Pedowitz, 1999;
Mangione, et al., 1996; Quigley, et al., 2000). Preliminary research on heart rate and
blood pressure during unloading show changes proportional to the amount of unloading
used, with most percentages of body weight support not eliciting clinically significant
changes in either parameter (Hargens, et al., 1999; Mangione, et al., 1996). When
comparing LBPP to harness-based systems, LBPP was found to be more comfortable at
all speeds and levels of unloading, however HR was lower using LBPP than the harness
system at equivalent levels of unloading (Ruckstuhl, et al., 2009). LBPP has also been
shown to decrease the perceived exertion experienced by the subject (Groppo, et al.,
2001).

Initial research examining LBPP devices suggests that it may be useful in the
rehabilitation of musculoskeletal and neurological conditions because it allows the
amount of weight being supported during ambulation to be varied, thus controlling the
amount of active muscle force and joint loading experienced by the lower extremities.
This may be useful for knee OA patients, who are often prescribed exercise programs but show low adherence because of pain from excessive joint loading. The effect of unloading, rate of patient adherence, and other variables of treatment using an LBPP treadmill on individuals with knee OA is currently unknown. Further, LBPP is currently used as a biomechanically acceptable method of acutely unloading an individual. While some researchers postulate that this may be equivalent to weight loss, there is currently no literature available on this comparison. To date, only one study has looked at the effect of body weight unloading on knee pain in knee OA (Mangione, et al., 1996). This study used a harness based system, and found pain responses to weight manipulation were highly variable; a significant relationship was not found between body weight support and knee pain (Mangione, et al., 1996). Patient walking time was variable, with most patients walking on the treadmill for only 6 minutes at an increasing incline (Mangione, et al., 1996). The average BMI of the study was 26.1 kg/m², considered only slightly overweight (25.0 - 29.9) (Mangione, et al., 1996). Patients with a higher BMI may experience more significant responses to unloading on the treadmill while walking, especially over longer time periods. The authors further suggest that while it is known that body weight support reduces joint reaction forces, joint acceleration changes during unloading are unknown, and this may influence knee pain as well (Mangione, et al., 1996). Further research is needed into the specific effect of LBPP on joint forces, knee pain, and rehabilitation of knee OA.
2.5 Outcome Measures

2.5.1 Accelerometry

Accelerometers can be used to measure acceleration about a joint. Accelerometry is a non-invasive, compact method of measuring acceleration about the knee. These devices have been used both for assessing global physical activity levels in OA patients (Farr, et al., 2008; Freedson, Melanson, & Sirard, 1998), as well as joint forces in patients with knee OA (Elvin, Elvin, & Arnoczky, 2007; Liikavainio, et al., 2010; Turcot, et al., 2008). It has been proven to be valid when compared to motion analysis systems, the gold standard for gait analysis (Currie, Rafferty, Duncan, Bell, & Evans, 1992; Mayagoitia, Nene, & Veltink, 2002). It is also considered reliable (Liikavainio, et al., 2007) and has been used with healthy and OA populations (Auvinet, et al., 2002; Liikavainio, et al., 2010; Turcot, et al., 2009). Accelerometers can be bone mounted or skin mounted using adhesive tape or an exoskeleton (Turcot, et al., 2008). While bone mounted accelerometers are most accurate, they are not widely used in a clinical setting (Turcot, et al., 2008). Skin mounted accelerometers (SMA’s) may produce artifact through vibration; however studies have shown that placement on the lower limb, adequate fixation and low equipment weight produce reliable and valid measurements (Liikavainio, et al., 2007; Turcot, et al., 2008) and this has been validated by directly comparing bone and skin mounted accelerometers (Lafortune, Henning, & Valiant, 1995). Currently, SMA’s attached directly to the skin using adhesive tape or on an exoskeleton are most commonly used in clinical trials, and no difference has been found between the two (Liikavainio, et al., 2010; Turcot, et al., 2008). Triaxial accelerometers can measure linear acceleration in three different planes: vertical or proximal-distal (PD), medial-lateral (ML), and anterior-posterior (AP). Accelerations at heel strike and at toe off are analyzed to assess the
impact of these loads on the knee. PD acceleration can represent the load transmission across the joint, with greater transmission at heel strike and toe off contributing to the degenerative process in OA (Turcot, et al., 2009). ML and AP acceleration is interpreted as shear force and instability in the knee joint, with greater values at heel strike representing more shear and instability, and this has been consistently observed in those with knee trauma such as ACL tears as well as those with knee OA (Turcot, et al., 2009; Yoshimura, et al., 2002). Those with knee OA tend to exhibit significantly higher knee acceleration than healthy controls in all 3 directions (Turcot, et al., 2009), however some studies have found differences only with higher intensity tasks than walking, such as stair-climbing (Liikavainio, et al., 2010). Turcot et al. (2008) found significantly greater accelerations in OA individuals as compared to asymptomatic controls only during heel strike, with ML tibial acceleration being significantly higher during walking. Differences in results may occur because of small sample sizes – the above study included only nine OA patients, and the varying range of disease severity – all patients that have evidence of OA, whether it be mild, moderate or severe, were included.

2.5.2 Short Questionnaire for Assessing Health-Enhancing Physical Activity (SQUASH) Questionnaire

Physical activity can be measured by direct or indirect means. Measuring self-reported patient physical activity levels using a survey can allow the categorization of physical activity conveniently and in an inexpensive way. The Short Questionnaire to Assess Health-enhancing Physical Activity (SQUASH) measures habitual physical activity levels of subjects and can be compared to national and international physical activity guidelines using a physical activity Compendium (Ainsworth, et al., 1993). The
SQUASH contains four sections: (A) commuting activities; (B) leisure time activities; (C) household activities; and (D) activities at work and school; and asks patients to recall the frequency (days per week), duration (average time per day) and intensity (light, moderate, or intense) of each activity (Wendel-Vos, Schuit, Saris, & Kromhout, 2003). The SQUASH Questionnaire is designed to capture information about activities performed that require >4 METs of intensity and the survey takes approximately 5 minutes to complete (Wendel-Vos, et al., 2003). It has been validated against accelerometry and proven reliable in a wide age range (18-65) (Wendel-Vos, et al., 2003). The SQUASH Questionnaire has been used with various populations, most recently in knee OA patients in an exercise intervention (Pisters, et al., 2010).

2.5.3 Visual Analog Scale

The Visual Analog Scale (VAS) is a tool for measuring the intensity of pain experienced by a patient, and consists of a 100 mm horizontal line with the two endpoints labeled as “no pain” and “worst possible pain” (Katz & Melzack, 1999). The distance from the endpoint “no pain” in millimeters corresponds to the patient’s numerical rating of pain severity on a scale of 0 – 100. Numerical pain measurements can then be compared from multiple VAS readings to assess the effect of pain-altering treatments. The VAS is a non-invasive, quick and effective method for measuring changes in a patient’s pain intensity (Katz & Melzack, 1999) and is recommended for use in clinical trials of knee OA by OMERACT and OARSI task forces (Pham, et al., 2003). It has been extensively used in clinical research (Bodian, Freedman, Hossain, Eisenkraft, & Beilin, 2001), and is a valid and reliable pain measurement tool (Katz & Melzack, 1999). However, the weakness of the VAS lies in its simplicity and uni-dimensionality, in that it
cannot measure other parameters of pain or discomfort, such as stiffness, which may contribute to a patient’s overall experience of pain (Katz & Melzack, 1999).

2.5.4 Knee injury and Osteoarthritis Outcome Score (KOOS) Knee Survey

The KOOS Knee Survey was developed for the standardized assessment of OA symptoms in the hip and/or knee joints, particularly in a young and active population (Roos, Roos, & Lohmander, 1999). The KOOS is a self-administered survey with the aim of evaluating symptoms important to OA patients without physician bias (Roos, Roos, Lohmander, Ekdahl, & Beynnon, 1998). Testing indicates that it is a valid, highly reliable and responsive measurement tool for evaluating changes after different OA interventions, and may even be more responsive in a young population than the WOMAC OA Index (Roos, et al., 1999; Roos, et al., 1998; Roos & Toksvig-Larsen, 2003). The KOOS Knee Survey has been used to evaluate populations after ACL tear, meniscal lesion, and total knee replacement (Roos, et al., 1999; Roos, et al., 1998; Roos & Toksvig-Larsen, 2003). The KOOS survey consists of 42 questions covering five dimensions, and contains the WOMAC within it: 1. Pain (9 questions); 2. Symptoms (7 questions); 3. Function in Daily Living (ADL) (17 questions); 4. Function in Sport and Recreation (5 questions); and Knee-Related Quality of Life (4 questions) (Roos, et al., 1998). The KOOS uses a Likert scale that ranges from 0 (no problems) to 4 (extreme problems) (Roos, et al., 1998). Scores are transformed to a scale ranging from 0-100, 0 representing extreme knee problems and 100 representing no knee problems.
3. HYPOTHESIS AND OBJECTIVES

3.1 Hypothesis

It is thought that weight loss positively affects knee pain in individuals with early-onset OA and alters knee joint loading via acceleration. The isolated effect of unloading on knee pain has been tested using a treadmill device that facilitates body weight support. The null hypothesis states that there will be no significant difference in VAS knee pain, KOOS Knee Survey scores and knee joint acceleration when comparing full weight bearing and Lower Body Positive-Pressure (LBPP) supported treadmill walking exercise in a young knee OA population.

3.2 Objectives

The purpose of this investigation was to examine the relationship between body weight and knee pain in an early-onset knee OA population using a LBPP treadmill that facilitates unloading of the lower extremities during walking. Specifically, the study had the following objectives:

1. Quantify the percentage of LBPP support required to alleviate knee pain during treadmill walking in a young knee OA population.
2. Quantify the degree of knee pain and function associated with full weight bearing treadmill walking and LBPP treadmill walking in a young knee OA population using the Visual Analog Scale (VAS) and the Knee injury and Osteoarthritis Outcomes Score (KOOS Knee Survey).
3. Quantify knee joint acceleration associated with full weight bearing treadmill walking, LBPP treadmill walking and walking on the walkway in a young knee OA population using wireless G-Link tri-axial accelerometers.
4. MATERIALS AND METHODS

4.1 Patient Population

For this prospective randomized study, twenty-four subjects were recruited. The study was carried out at the David & Ruth Asper Research Centre, Pan Am Clinic Foundation in Winnipeg, Manitoba. Ethics approval was obtained from the University of Manitoba. Approval for research access was obtained from the Winnipeg Regional Health Authority. Patient inclusion criteria consisted of the following: 1. Age 35-59 years; 2. Body mass index (BMI) of >25 kg/m² (Felson, 1996b); 3. Radiographic evidence of mild to moderate knee OA, read from the radiology reports; and 4. Knee pain when performing normal activities of daily living such as walking, squatting or kneeling. Criteria for exclusion of study subjects included: 1. Radiographic evidence of severe OA; 2. A recent history (within the last year) of traumatic hip, knee or ankle injury or surgery; and 3. History of cardiovascular disease, or screening positive for rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, chronic reactive arthritis, or experiencing renal problems that require hemodialysis or peritoneal dialysis (Neogi, et al., 2009). The study was advertised using print media, posters, word-of-mouth and through referral from the MRI technicians at Pan Am Clinic. Respondents to print media and posters were initially contacted by phone to assess preliminary eligibility for the study. If the participant met the inclusion criteria, they were then scheduled for an intake session where eligibility was verified, then immediately followed by the first testing session.
4.2 Imaging

Weight-bearing antero-posterior radiographs with both knees in 15° of flexion were taken for all subjects. Radiographs were obtained using a Basic Radiographic System (Siemens, Erlangen, Germany) at 70 KV and 10 mA, with a film focus distance of 1.4 m. All radiographs were interpreted by a musculoskeletal radiologist (M.D.) within a period of 5 days. The radiologist scored knee OA as mild, moderate, or severe.

4.3 Intake

At the first session, participants completed informed consent and participant information forms. The following forms were asked to be filled out: 1. Participant Information Form; 2. Knee Demographic Form; 3. Short Questionnaire to Assess Health Enhancing Physical Activity (SQUASH); and 4. KOOS Knee Survey. The Participant Information Form captured patient demographics including age, previous history of injury, dominant hand and leg, and basic patient information including name, address and phone number. The Knee Demographic Form obtained details about knee symptoms and knee pain experienced by the patient, as well as previous injury, activities, treatments, general health and any medication taken. The SQUASH Knee Survey collected more detailed information about physical activity levels, and the KOOS Knee Survey categorized knee pain, and physical function. The KOOS Knee Survey was filled out prior to the first treadmill walking session, one week later at the start of the second treadmill walking session, and one week after this final treadmill session. Subjects were given a Garmin Forerunner 405 HR monitor to wear during all treadmill walking sessions. The experimenter wore the watch and determined resting heart rate of the
subject. This was used to determine the patient’s heart rate range for treadmill walking (50-65% of maximal heart rate to represent a moderate level of intensity). Height in meters (to two decimal places) and weight in kilograms was measured using the Seca 700 Beam Scale with measuring rod (Seca, Birmingham, UK). Height and weight data were used to calculate BMI. Leg alignment was measured with the patient lying on a plinth with legs together. If both knees and medial malleoli were touching, alignment was recorded as neutral. If medial malleoli were touching and the space between the knees was greater than 1 cm when measured using a measuring tape, alignment was recorded as varus, and if the knees were touching and the space between the medial malleoli was greater than 1 cm, alignment was recorded as varus. This grading criteria has been used with sporting populations before (Witvrouw, Lysens, Bellemans, Cambier, & Vanderstraeten, 2000). Limb length was measured, as the distance from the inferior portion of the anterior superior iliac spine to the inferior aspect of the medial malleolus in centimeters, using a flexible measuring tape (Golightly, et al., 2007). The length of both limbs was recorded. Thigh girth was then measured as the circumference of the thigh musculature 6 inches proximal to the superior pole of the patella with the same measuring tape (Wyatt, et al., 2001). Patients were scheduled for radiographs at Pan Am Clinic. The VAS was introduced and patients were instructed on how to record their level of pain using this scale, during walking on a newly developed treadmill device called the G-trainer (Alter-G, Menlo Park CA). Patients were then given treadmill specific shorts to wear during treadmill walking, which were worn over their shorts, and were familiarized with the treadmill walking protocol prior to beginning the walking session. After testing, patients were scheduled for the final treadmill testing session, to occur approximately one week later.
4.4 Testing Sessions

Following pilot testing to refine treadmill walking methodologies, subjects completed 2 treadmill walking sessions, and 2 walkway walking sessions. During treadmill testing, subjects were instructed to walk at a speed of 1.4 m/s at 0º incline (Browning & Kram, 2007) for a period of 25 minutes. The initial 5 minutes of each session was used as a warm-up to allow the subject to reach their target heart rate zone (50% - 65% of maximal heart rate), reach the predetermined speed, and adjust to walking on the treadmill’s belt surface. Subjects completed one session of full weight bearing walking and one session of LBPP-supported walking. The percentage of LBPP used in the weight-supported session was systematically increased by 5% increments every minute until pain was eliminated, a leveling off in pain was reached according to VAS measures, or until 25% support was reached (Figure 2). This percent of LBPP was confirmed by 2 further increases in LBPP per minute, before returning to the determined percentage for the remainder of the treadmill walking session. During each new level of unloading, 20 seconds of accelerometry data were recorded. The LBPP was a chamber pressure that was high enough to alleviate or substantially lower knee pain for the duration of the subject’s walk. For the remainder of the walk, HR, pain using VAS and accelerometry were recorded every 5 minutes. The order of testing sessions was randomized, and subjects were blinded to the percentage of LBPP used during both testing sessions. Twenty seconds of accelerometry data were also recorded during full weight bearing walking on a 12m wooden walkway, to compare to treadmill walking. Two trials of walking at a self-selected comfortable speed, and 2 trials of walking at a self-selected fast speed were collected.
4.5 Accelerometry

In the current study, wireless G-Link accelerometers were used to assess joint load about the knee during different percentages of un-weighting (Figure 3a). Accelerometers were attached to the skin of both of the patient’s knees prior to treadmill walking, and were worn for the duration of both treadmill walking sessions. Figure 3b shows the placement of the accelerometers. Accelerometers were placed on the medial surface of the tibia, at 20% of the distance between the medial malleolus and the medial joint space (Liikavainio, et al., 2007) after being turned on. The distance from medial joint line to the tubercle of the medial malleolus was measured and 20% of the distance from the joint line was calculated, and marked on the patient’s skin with pen. The accelerometer was then placed with blue G-Link strip facing to the right on both knees, and with the transmitter turned laterally to prevent contact between accelerometer transmitters during walking. A strip of double-sided tape was placed on the underside of each accelerometer, and two strips of adhesive sports tape were wrapped horizontally around the top and bottom of the accelerometer. The procedure was then repeated for the other leg. Node 386 was always placed on the right leg and Node 402 on the left leg. Prior to entering the treadmill apparatus, patients were asked to swing their legs systematically in the three different planes that the accelerometer records in (Z or proximal-distal, X or medial-lateral, and Y or anterior-posterior). Using Agile Link software for the G-Link accelerometers (Microstrain Inc., Williston, VT), accelerometers were streamed live to verify the connection, and to determine which graphing line corresponded with which plane of movement during the single plane movements. This sequence was repeated with the other leg and streaming of the other node. Accelerometers were set at a sampling frequency of 1024 Hz, and 20 seconds of data
were collected with each triggered session of data logging. After the treadmill session and collection of data, the trigger sessions were downloaded from the accelerometers into Microsoft Office Excel 2007 files onto the computer. Data were partitioned and saved according to left or right leg, percent of LBPP and plane of movement (X, Y, or Z). The excel files were then saved as CSV comma delimited files, and exported to Sigview (Signal Lab, Pforzheim, Germany). Each trigger session was filtered in Sigview using a band pass range of 0.5 to 25 Hz. This ensured that vibration and artifact were removed from the accelerometer recording. Once filtered, gait data were exported back to Excel and 5 steps of consecutive gait data were averaged to be analyzed, not including outliers. The first and last step recorded by the accelerometer were not used. Gait data in 3 directions, in line with previous accelerometry research on OA (Turcot, et al., 2008) were extracted – proximal-distal (PD), anterior-posterior (AP) and medial-lateral (ML) directions. The range of acceleration at heel strike, measured as the change in acceleration from Peak-to-Peak (PP), was measured for all three directions. Range of acceleration at toe off (PP acceleration) was extracted for PD and ML directions, and the initial impact of heel strike, known as the Initial Peak Acceleration (IPA) for the PD direction was also extracted.

4.6 G-Trainer Treadmill

Once transmission of the accelerometers was verified, patients were helped into the opening of the treadmill. The location of the subject’s greater trochanter was determined and the midpoints of the upper bars of the treadmill apparatus were positioned to coincide with this height. The subject lifted the front bars of the treadmill apparatus and positioned it between two notches at the predetermined height, while the
experimenter lifted the back bars and placed it between the same notches. Safety latches were then closed to keep the bars, which make up the top part of the treadmill cage, in place. The subject’s shorts were zipped in to the treadmill opening. The treadmill was then calibrated for the individual using an on-board computer, where the patient was instructed to remain standing and keep all weight on their feet. After calibration, the walking protocol was started. The subject walked for 5 minutes at 1.4 m/s (3.1 mph) as part of a warm up. Subjects were allowed to hold on to the front or sides of the treadmill frame for support or stabilization. Heart rate, knee pain in the affected knee using a VAS, and knee acceleration were assessed at 5 minutes. The VAS was placed on a clipboard and placed in front of the patient, who was also handed a pen to mark their level of pain. At 5 minutes, either full weight-bearing was maintained during the full weight bearing walking session, or LBPP was initiated in the LBPP walking session.

4.7 Full Weight Bearing Treadmill Walking

After the 5 minute warm-up, the patient continued walking at 1.4 m/s with 0° incline for another 20 minutes. After every 5 minute interval, knee pain was assessed using a new VAS. Patients were not able to see their previous VAS markings. Heart rate and knee acceleration data were also recorded. After 25 minutes, the treadmill was stopped, and patients were unzipped from the device. The safety was unlatched, and the bars were unhitched from the notches with the patient guiding the bars in the front and the experimenter lowering the bars in the back. Patients were then helped out of the treadmill. Subjects were then asked to walk across a walkway to gather accelerometry data comparing treadmill to walkway. Subjects made 2 passes at a self-selected
comfortable and 2 passes at a self-selected fast speed across the wooden walkway, and
accelerometry data during each of these trials was recorded. If this was the final treadmill
session, subjects were given a KOOS Knee Survey with prepaid envelope to fill out in
one week’s time and mail to the experimenter.

4.8 LBPP-Supported Treadmill Walking
At 4.5 minutes into the warm-up, the first accelerometry session was triggered to gather
data about full weight-bearing. Figure 2 shows the unloading protocol: 5% every minute,
followed by the triggering of an accelerometer session, and knee pain rating on VAS. The
percentage of LBPP used in the weight-supported session was systematically increased
by 5% increments every minute until a leveling off in pain was reached according to VAS
measures, or until 25% support was reached. This percent of LBPP was confirmed by 2
further increases in LBPP per minute, before returning to the determined percentage for
the remainder of the treadmill walking session. The above sequence was repeated every
minute during the unloading process (unload, trigger accelerometer, assess knee pain on
VAS). The maximum unloading for the duration of the session was 25%, with some
subjects briefly walking at 30 and 35% unloading to verify the level of body weight
support. LBPP was kept constant for the rest of the session after the level of unloading
was determined using the above protocol. Heart rate and knee acceleration recordings
were taken every 5 minutes, and after the determination of LBPP, pain was also measured
using VAS at 5 minute intervals. After 25 minutes, the treadmill was stopped and the
patient exited the treadmill using the same method as described above for weight bearing
treadmill walking.
4.9 Sample Size

Previous research using the VAS indicates that 13 mm is the minimum clinically significant difference (Todd, Funk, Funk, & Bonacci, 1996). Research examining acute pain illustrates a standard deviation of 19 on the VAS (Todd, et al., 1996). In clinical research, a power of at least 80% is required for the study to be deemed acceptable (Hassard, 1991). A power of 90% was used for this study. Using an $\alpha = 0.05$ (two-tailed) and $\beta = 0.10$, as well as a sample size increase of 20% to account for withdrawal from the study, the estimated sample size was:

$$N = 1\{(1.96+1.28)\sqrt{19/13}\}^2 \times 1.20 = 26.91$$ or 27 total participants required for this study.

4.10 Statistical Analysis

Descriptive statistics including means, standard errors, standard deviations, and ranges were calculated for the group. Paired t-tests were used to compare anthropometry (including leg length, thigh girth) and heart rate during walking and KOOS Knee Survey data. Repeated Measures Analysis of Variance (ANOVA) were used to compare KOOS Knee Survey data, VAS scores taken every 5 minutes during walking, and each subject’s knee acceleration data, to compare linear accelerations in PD, AP, and ML directions during walkway walking, full weight-bearing, and the different LBPP conditions. Least Significant Difference pair-wise comparisons were used to look for significant differences in post-hoc analysis. Differences were considered statistically significant if $p < 0.05$. Parametric statistics were used for analysis because there were equal and consistent intervals between data groups for comparison. Regression analysis was used to examine the relationship between body weight, knee pain on the VAS, knee acceleration and scores on the KOOS Knee Survey. Pearson product-moment coefficient of
correlation testing was used to examine the relationships between scoring on the KOOS Knee Survey, BMI and body weight, VAS scores during full weight-bearing treadmill walking, and the percentage of LBPP required for the subject to walk pain-free on the treadmill. Microsoft Office Excel 2007 with the Analysis ToolPak add-in and SPSS v.17 was used for data analysis.
5. RESULTS

5.1 Patient Population

The population of interest was a younger, symptomatic knee OA population that was still active but suffered from morbidity. Twenty-four participants were enrolled in the study. Two participants were excluded after the initial session, one for cognitive impairment, and one after radiological evaluation revealed no evidence of knee OA. Twenty-two participants successfully completed the testing sessions.

Subject descriptive data, body anthropometry and physical activity data are summarized in Table 1. The average age of the population was 52.9 years, with an average body weight of 93.7 kg, height of 1.7 m, and a BMI of 33.6 kg/m². Seventeen females and 5 males participated in the study. Knee alignment was measured, and 2 patients were found to have neutral alignment, 7 patients were recorded as having varus alignment, and 13 patients were recorded as having valgus alignment. All patients reported painful knees. Nine participants demonstrated bilateral knee OA, and 13 demonstrated unilateral knee OA. In cases of bilateral knee OA, the worse affected knee was considered the test knee, in line with previous research (Liikavainio, et al., 2010). The majority of participants had pain in their right knee (14 right, 8 left), with all patients except one exhibiting one of the following: medial knee compartment degeneration, degeneration of the same magnitude in both compartments or degeneration in both compartments with worse medial degeneration.

Leg length and thigh girth were both measured to examine abnormal differences between affected and unaffected legs. There was no significant difference in leg length among patients (Paired t-test p = 0.79). Patients tended to have smaller thigh girths on the
side of the affected knee, however this was not significant (Paired t-test, p = 0.34). The results for both leg length and thigh girth remained the same when controlling for type of OA (unilateral vs bilateral; Paired t-test, p = 0.15).

The majority of patients had been experiencing knee problems for more than 3 years, with the shortest length of time being 9 months since the start of knee pain. Half of the patients had previously suffered a serious knee injury and half had also undergone some form of knee surgery in the past (not necessarily the same individuals who had experienced knee injury). The time of the injury was not recorded. Overall, 15 participants had suffered from knee injury, had undergone surgery, or both.

Participants self-reported high levels of activity. The average SQUASH score was 5626, with scores ranging from 1620 to 15,360. Patients recorded on average 2596 minutes of activity per week, with 73% (1886 minutes) of their time spent in light activity between 2 and 4 Metabolic Equivalents (METs), 15% (403 minutes) spent in moderate intensity (4-6 METs) activity, and 12% (308 minutes) spent in high intensity (6+ METs) activity. Two group outliers were observed to spend over 2000 minutes per week in moderate and intense physical activity (double the next highest score). Once these two scores were removed, the average time spent in moderate and intense physical activity per week was estimated at 544 minutes (9 hours).

During treadmill walking, heart rate was maintained between 50 and 65% of the patient’s heart rate maximum, the patient’s function and treadmill speed permitting. Average heart rate during full weight-bearing walking and LBPP walking was 112 and 110 bpm, respectively. There was no significant difference between full weight-bearing and LBPP heart rate (Paired t-test p = 0.15).
Patients were un-weighted to the point of maximal pain relief (reaching 0 on the pain scale), or when changes in pain levels plateaued. Patients were un-weighted on average 12.3% of body weight, with the most common level of un-weighting being 10%. There was a weak correlation between the level of un-weighting and the pain relief experienced by patients on the treadmill ($r = 0.31$), with higher levels of un-weighting associated with greater pain relief. Subjects maintained a speed, where possible, of 3.1 mph on the treadmill. Six subjects were unable to ambulate at this speed and their speed was lowered in 0.1 mph intervals until they could successfully complete the session. These subjects still maintained a heart rate between 50 and 65% of their maximum heart rate range. The lowest speed maintained by any participant was 1.4 mph, with a pain level of 43/100 during full weight-bearing.

5.2 Knee Pain and KOOS Function

Knee pain data during full and partial weight bearing sessions are summarized in Table 2. Knee pain was measured during treadmill walking using a 0 – 100 mm Visual Analog Scale (VAS). Average knee pain during full weight-bearing treadmill walking was 27.7 mm over the 25-minute session. Figure 4 shows differences in pain as experienced during full weight-bearing and LBPP treadmill walking. Pain increased significantly over the entire full weight-bearing walking session (ANOVA $p = 0.002$) and significant increases were seen between minutes 5 and 10, and minutes 10 and 15 (ANOVA $p = 0.029$).

During unloading, pain decreased significantly only when the patient was unloaded at 10% LBPP (ANOVA $p = 0.035$). There was a significant difference between pain change over the full weight-bearing walking session and pain change over the LBPP
treadmill walking session (Paired t-test p = 0.03) with pain increasing more so in the full weight-bearing session. Importantly, knee pain did not significantly increase during the treadmill walking session when the patient was unloaded (ANOVA p > 0.05). This is significantly different from the full weight-bearing condition.

KOOS scores are summarized in Table 3. Participants recorded knee pain and function on the KOOS survey at three time points. Scores in the KOOS Survey can range from 0 (complete disability) to 100 (no disability) for each category – Pain, Symptoms, Function in Daily Living, Sports/Recreation and Quality of Life. Response rate to the first 2 surveys was 100%. Patients were asked to complete and mail in a third and final KOOS survey one week after the last treadmill walking session. Response rate for the last survey was 65%. Of the individuals who did not respond to the final survey, only 2 differed from the sample population, with one having significantly lower and one having significantly higher scores on the previous 2 KOOS surveys (Paired t-test p = 0.008; p = 0.014). Figure 5 illustrates that KOOS scores did not significantly differ between the first, second or third survey (ANOVA p > 0.05). When individuals who did not respond to the final KOOS survey were excluded from analysis, there was a significant decline in Function in Daily Living scores from the first to the second survey (ANOVA p = 0.029) and a significant improvement in Quality of Life from the second to the third survey (ANOVA p = 0.027). There was a moderate correlation between body weight and the KOOS, with greater values of body weight correlating with lower scores in all KOOS categories (indicative of greater disability). Correlations between body weight and KOOS category ranged from -0.18 to -0.51. Knee pain and KOOS scores were also correlated. Figure 6 shows a moderate negative correlation between maximum VAS pain during full weight-bearing treadmill walking and average KOOS pain scores (r = -0.57; Regression p =
High pain scores are indicative of lower KOOS scores (lower KOOS scores indicating greater levels of disability). Average KOOS was also correlated with average pain during full weight-bearing walking ($r = -0.53$; Regression $p = 0.02$), but not with initial pain scores in either LBPP or full weight-bearing conditions. Function in Daily Living scores recorded on the KOOS were also significantly correlated with pain scores on the VAS (Regression $p = 0.04$), with higher pain scores indicative of lower function as recorded on the KOOS ($r = -0.46$).

5.3 Knee Acceleration

Accelerometry data for both full and partial weight bearing treadmill sessions for the PD direction are summarized in Table 4A, 4B, and 4C. Acceleration was measured in 3 planes during walking. In the proximal-distal (PD) direction, variables recorded were the Initial Peak Acceleration (IPA), the Peak-to-Peak (PP) acceleration at heel strike to flat-foot (which measures the range of acceleration from heel strike to flat foot) and the Peak-to-Peak (PP) acceleration at toe off (which measures the range of acceleration from push-off to when the foot is off the ground) in both affected and unaffected knees. In the anterior-posterior (AP) direction, Peak-to-Peak (PP) acceleration at heel strike to flat-foot in both affected and unaffected knees was recorded, and accelerometry data for this are summarized in Table 5. Accelerometry data for the ML direction are summarized in Table 6A & 6B. In the medial-lateral (ML) direction, Peak-to-Peak (PP) acceleration at heel strike to flat-foot and toe off in both affected and unaffected knees was recorded. Heel strike to flat-foot will be referred to as heel strike in this study. Differences in acceleration were analyzed for 7 conditions: at full weight-bearing on the treadmill, at 5, 10, 15 and 20% LBPP, and during two trials of walking on a walkway at a comfortable
and a fast speed. Accelerometry data are available for 20 participants; 2 participants were excluded, having not worn accelerometers during their initial walking sessions. For 20% LBPP, data from 14 participants were available for analysis (the total of participants to ambulate at this level).

5.3.1 Knee Acceleration on the Treadmill

For PD acceleration, Figure 7a shows a significant decrease in IPA in the affected knee as LBPP increases, with significant differences seen between 5% LBPP and higher levels of un-weighting (ANOVA p = 0.026). This is also seen in the unaffected knee, with differences between 20% LBPP and the following: full weight-bearing and 5% LBPP (ANOVA p = 0.028). Figure 7b shows a similar pattern when examining heel strike, with knee acceleration significantly decreasing with LBPP in both knees (ANOVA p = 0.034). A more pronounced decrease in acceleration at toe off is seen in Figure 7c with LBPP (ANOVA p = 0.016), where full weight-bearing and 5% LBPP knee acceleration is significantly lower than other walking conditions. In the AP direction, no difference in knee acceleration at heel strike was seen between treadmill LBPP conditions in the affected knee (ANOVA p > 0.05). However, Figure 8 shows that the unaffected knee did display significant decreases in PP heel strike with LBPP (ANOVA p = 0.042), with differences between 5% LBPP and greater levels of un-weighting. Figure 9a also shows a decrease in knee acceleration in the ML direction with LBPP (ANOVA p = 0.018), however this is observed only in the affected knee. At toe off, knee acceleration decreases with LBPP in both knees, as shown in Figure 9b.
5.3.2 Knee Acceleration on the Walkway

Both knees show a significant difference in all directions (except in the ML direction in the unaffected knee during heel strike) between fast walking on the walkway and all other conditions (ANOVA p = 0.022), with accelerations being much higher during fast walking. Walking at a comfortable speed on the walkway resulted in significantly lower knee accelerations in all three parameters analyzed in the PD direction (ANOVA p = 0.034), and in the AP direction in the affected knee (ANOVA p = 0.047) than walking at a fast speed and treadmill walking. Comparison between knees did not result in significant differences during walkway or treadmill walking for this patient population (ANOVA p > 0.05).

5.3.3 Knee Acceleration, Body Weight and Knee Pain Relationship

Figure 10 shows a significant moderate correlation between body weight and PD knee acceleration, with comfortable walkway PP heel strike acceleration increasing as body weight increases (r = 0.50; Regression p = 0.02). The relationship between PP heel strike knee acceleration and BMI approached significance (Regression p = 0.051). There was a significant relationship between body weight and ML acceleration, with greater heel strike knee acceleration during fast walking on the walkway seen at higher body weights (Regression p = 0.02). There was no relationship between BMI and any ML knee acceleration conditions. There was a significant positive relationship between BMI and resultant heel strike acceleration when fast walking on a walkway (Regression p = 0.039). Body weight and BMI were not related to any other condition of resultant acceleration. No significant relationship was found when comparing body weight or BMI to the change in acceleration at heel strike and toe off with LBPP (Regression, p > 0.05).
Pain on the VAS during full weight-bearing was not associated with PP heel strike in any direction (Regression p > 0.05). Pain as recorded on the KOOS Knee Survey was also not associated with PP heel strike in any direction (Regression p > 0.05). Pain on the VAS during treadmill walking and the pain category score on the KOOS were not related to resultant heel strike acceleration (Regression p > 0.05).
6. TABLES AND FIGURES
Table 1. Anthropometry

<table>
<thead>
<tr>
<th>Anthropometry</th>
<th>Total Mean (SD)</th>
<th>Unilateral Mean (SD)</th>
<th>Bilateral Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>52.9 (5.9)</td>
<td>52.6 (6.0)</td>
<td>53.2 (7.4)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.68 (0.1)</td>
<td>1.68 (0.1)</td>
<td>1.66 (0.1)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>93.7 (18.8)</td>
<td>87.8 (14.3)</td>
<td>102.2 (21.3)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>33.6 (6.4)</td>
<td>31.3 (5.3)</td>
<td>36.9 (6.8)</td>
</tr>
<tr>
<td>Leg Length Difference (cm)</td>
<td>1.0 (1.1)</td>
<td>0.8 (0.7)</td>
<td>1.2 (1.2)</td>
</tr>
<tr>
<td>Thigh Girth Difference (cm)</td>
<td>1.3 (1.0)</td>
<td>1.3 (0.6)</td>
<td>1.4 (1.3)</td>
</tr>
<tr>
<td>Activity Level (min/week)</td>
<td>543.5 (297.4)</td>
<td>532.9 (323.8)</td>
<td>569.0 (253.7)</td>
</tr>
<tr>
<td>FWB Heart Rate (bpm)</td>
<td>112 (14.8)</td>
<td>109 (15.5)</td>
<td>116 (15.0)</td>
</tr>
<tr>
<td>LBPP Heart Rate (bpm)</td>
<td>110 (14.5)</td>
<td>108 (15.5)</td>
<td>114 (14.3)</td>
</tr>
</tbody>
</table>

Anthropometry of the population is presented. Values are given for the total population, unilateral osteoarthritis (OA) group and bilateral OA group, and indicate a homogenous patient group, representative of an overweight/obese early-onset knee OA population.
Table 2. Knee Pain during Treadmill Walking

<table>
<thead>
<tr>
<th>LBPP Amount</th>
<th>Mean Pain (SD)</th>
<th>LBPP Session Time</th>
<th>Mean Pain (SD)</th>
<th>FWB Session Time</th>
<th>Mean Pain (SD)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBPP 0%</td>
<td>21.2 (17.5)</td>
<td>LBPP 5 min</td>
<td>21.2 (17.5)</td>
<td>FWB 5 min</td>
<td>20.9 (17.1)</td>
</tr>
<tr>
<td>LBPP 5%</td>
<td>22.9 (15.4)</td>
<td>LBPP 10 min</td>
<td>19.6 (18.6)</td>
<td>FWB 10 min</td>
<td>14.6 (16.5)</td>
</tr>
<tr>
<td>LBPP 10%</td>
<td>20.6 (16.4)</td>
<td>LBPP 15 min</td>
<td>21.5 (20.5)</td>
<td>FWB 15 min</td>
<td>27.9 (17.8)</td>
</tr>
<tr>
<td>LBPP 15%</td>
<td>21.8 (17.7)</td>
<td>LBPP 20 min</td>
<td>23.2 (22.4)</td>
<td>FWB 20 min</td>
<td>31.4 (21.5)</td>
</tr>
<tr>
<td>LBPP 20%</td>
<td>18.6 (19.7)</td>
<td>LBPP 25 min</td>
<td>26.4 (24.1)</td>
<td>FWB 25 min</td>
<td>33.9 (24.3)</td>
</tr>
</tbody>
</table>

Knee pain as measured on the Visual Analog Scale (VAS) (mm) is presented for each unloading interval (5, 10, 15 and 20%), and for the entire Lower Body Positive-Pressure (LBPP) and full weight-bearing (FWB) session, in 5 minute intervals. * indicates significance from pain at 5 minutes (immediately after warm-up) (p < 0.05)
Table 3. KOOS Knee Survey Scores

<table>
<thead>
<tr>
<th>KOOS Category</th>
<th>KOOS 1 (SD)</th>
<th>KOOS 2 (SD)</th>
<th>KOOS 3 (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>48.9 (16.0)</td>
<td>51.0 (15.9)</td>
<td>54.6 (16.6)</td>
</tr>
<tr>
<td>Symptoms</td>
<td>48.2 (17.5)</td>
<td>46.2 (16.6)</td>
<td>53.6 (17.6)</td>
</tr>
<tr>
<td>Function in Daily Living</td>
<td>59.5 (20.8)</td>
<td>56.9 (17.9)</td>
<td>63.2 (20.1)</td>
</tr>
<tr>
<td>Sports/Recreation</td>
<td>22.3 (23.0)</td>
<td>23.7 (18.1)</td>
<td>29.2 (27.9)</td>
</tr>
<tr>
<td>Quality of Life</td>
<td>28.4 (22.1)</td>
<td>29.3 (17.6)</td>
<td>35.9 (20.3)</td>
</tr>
</tbody>
</table>

Knee injury and Osteoarthritis Outcome (KOOS) knee function scores are presented for each category for the first, second, and third KOOS knee survey. No significant change in scores was seen.
### Table 4a. Proximal-Distal Initial Peak Impact Knee Acceleration during Walking

<table>
<thead>
<tr>
<th>Affected Knee Walking Condition</th>
<th>Mean (SD)</th>
<th>Unaffected Knee Walking Condition</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FWB</td>
<td>1.73 (0.70)</td>
<td>FWB</td>
<td>1.76 (0.79)</td>
</tr>
<tr>
<td>5% LBPP</td>
<td>1.82 (0.79)</td>
<td>5% LBPP</td>
<td>1.73 (0.80)</td>
</tr>
<tr>
<td>10% LBPP</td>
<td>1.68 (0.75) *</td>
<td>10% LBPP</td>
<td>1.67 (0.76)</td>
</tr>
<tr>
<td>15% LBPP</td>
<td>1.64 (0.75) *</td>
<td>15% LBPP</td>
<td>1.61 (0.70)*</td>
</tr>
<tr>
<td>20% LBPP</td>
<td>1.70 (0.86) *</td>
<td>20% LBPP</td>
<td>1.66 (0.83)*+</td>
</tr>
<tr>
<td>Comfortable Walking</td>
<td>1.29 (0.66)*+</td>
<td>Comfortable Walking</td>
<td>1.16 (0.59)*+Δ</td>
</tr>
<tr>
<td>Fast Walking</td>
<td>2.34 (0.97)*+</td>
<td>Fast Walking</td>
<td>2.37 (0.88)*+Δ</td>
</tr>
</tbody>
</table>

A: Initial Peak Acceleration (IPA) in the proximal-distal (PD) plane during different walking conditions. * indicates significant when compared to FWB; + indicates significant when compared to 5% LBPP; Δ indicates significant when compared to 10% LBPP. FWB – full weight-bearing; LBPP – Lower Body Positive-Pressure
Table 4b. Proximal-Distal Knee Acceleration at Heel Strike during Walking

<table>
<thead>
<tr>
<th>Affected Knee Walking Condition</th>
<th>Mean (SD)</th>
<th>Unaffected Knee Walking Condition</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FWB</td>
<td>2.58 (0.88)</td>
<td>FWB</td>
<td>2.66 (1.00)</td>
</tr>
<tr>
<td>5% LBPP</td>
<td>2.69 (1.00)</td>
<td>5% LBPP</td>
<td>2.67 (1.06)</td>
</tr>
<tr>
<td>10% LBPP</td>
<td>2.50 (0.97) *</td>
<td>10% LBPP</td>
<td>2.58 (1.00)</td>
</tr>
<tr>
<td>15% LBPP</td>
<td>2.43 (0.94) **</td>
<td>15% LBPP</td>
<td>2.47 (0.92) **</td>
</tr>
<tr>
<td>20% LBPP</td>
<td>2.50 (1.10)</td>
<td>20% LBPP</td>
<td>2.53 (1.06) **</td>
</tr>
<tr>
<td>Comfortable Walking</td>
<td>1.93 (0.87) **</td>
<td>Comfortable Walking</td>
<td>1.84 (0.79) **</td>
</tr>
<tr>
<td>Fast Walking</td>
<td>3.14 (1.51) ^</td>
<td>Fast Walking</td>
<td>3.48 (1.20) ^</td>
</tr>
</tbody>
</table>

B: Peak-to-Peak (PP) heel strike knee acceleration in the proximal-distal (PD) plane during different walking conditions. * indicates significant when compared to FWB; + indicates significant when compared to 5% LBPP; ^ indicates significant when compared to 10% LBPP. FWB – full weight-bearing; LBPP – Lower Body Positive-Pressure.
### Table 4c. Proximal-Distal Knee Acceleration at Toe Off during Walking

<table>
<thead>
<tr>
<th>Affected Knee Walking Condition</th>
<th>Mean (SD)</th>
<th>Unaffected Knee Walking Condition</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FWB</td>
<td>1.92 (0.40)</td>
<td>FWB</td>
<td>1.89 (0.39)</td>
</tr>
<tr>
<td>5% LBPP</td>
<td>1.87 (0.37)</td>
<td>5% LBPP</td>
<td>1.89 (0.40)</td>
</tr>
<tr>
<td>10% LBPP</td>
<td>1.85 (0.36)</td>
<td>10% LBPP</td>
<td>1.92 (0.34)</td>
</tr>
<tr>
<td>15% LBPP</td>
<td>1.79 (0.33)* +</td>
<td>15% LBPP</td>
<td>1.80 (0.35)* +Δ</td>
</tr>
<tr>
<td>20% LBPP</td>
<td>1.73 (0.38)* +Δ</td>
<td>20% LBPP</td>
<td>1.80 (0.35)* Δ</td>
</tr>
<tr>
<td>Comfortable Walking</td>
<td>1.60 (0.34)* +Δ</td>
<td>Comfortable Walking</td>
<td>1.68 (0.46)* +Δ</td>
</tr>
<tr>
<td>Fast Walking</td>
<td>2.31 (0.51)* +Δ</td>
<td>Fast Walking</td>
<td>2.30 (0.53)* +Δ</td>
</tr>
</tbody>
</table>

**C**: Peak-to-Peak (PP) toe off knee acceleration in the proximal-distal (PD) plane during different walking conditions. * indicates significant when compared to FWB; + indicates significant when compared to 5% LBPP; Δ indicates significant when compared to 10% LBPP. FWB – full weight-bearing; LBPP – Lower Body Positive-Pressure
Table 5. Anterior-Posterior Knee Acceleration at Heel Strike during Walking

<table>
<thead>
<tr>
<th>Affected Knee Walking Condition</th>
<th>Mean (SD)</th>
<th>Unaffected Knee Walking Condition</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FWB</td>
<td>1.83 (0.49)</td>
<td>FWB</td>
<td>1.78 (0.53)</td>
</tr>
<tr>
<td>5% LBPP</td>
<td>1.83 (0.54)</td>
<td>5% LBPP</td>
<td>1.84 (0.51)</td>
</tr>
<tr>
<td>10% LBPP</td>
<td>1.84 (0.54)</td>
<td>10% LBPP</td>
<td>1.85 (0.51)</td>
</tr>
<tr>
<td>15% LBPP</td>
<td>1.79 (0.53)</td>
<td>15% LBPP</td>
<td>1.78 (0.46) *Δ</td>
</tr>
<tr>
<td>20% LBPP</td>
<td>1.88 (0.45)</td>
<td>20% LBPP</td>
<td>1.79 (0.50)</td>
</tr>
<tr>
<td>Comfortable Walking</td>
<td>1.48 (0.45) *Δ</td>
<td>Comfortable Walking</td>
<td>1.64 (0.43)</td>
</tr>
<tr>
<td>Fast Walking</td>
<td>2.25 (0.60) *Δ</td>
<td>Fast Walking</td>
<td>2.42 (0.54) *Δ</td>
</tr>
</tbody>
</table>

Peak-to-Peak (PP) heel strike knee acceleration in the anterior-posterior (AP) plane during different walking conditions. * indicates significant when compared to FWB; + indicates significant when compared to 5% LBPP; Δ indicates significant when compared to 10% LBPP. FWB – full weight-bearing; LBPP – Lower Body Positive-Pressure
Table 6a. Medial-Lateral Knee Acceleration at Heel Strike during Walking

<table>
<thead>
<tr>
<th>Affected Knee Walking Condition</th>
<th>Mean (SD)</th>
<th>Unaffected Knee Walking Condition</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FWB</td>
<td>1.56 (0.67)</td>
<td>FWB</td>
<td>1.65 (0.53)</td>
</tr>
<tr>
<td>5% LBPP</td>
<td>1.60 (0.66)</td>
<td>5% LBPP</td>
<td>1.52 (0.45)</td>
</tr>
<tr>
<td>10% LBPP</td>
<td>1.56 (0.64)</td>
<td>10% LBPP</td>
<td>1.56 (0.52)</td>
</tr>
<tr>
<td>15% LBPP</td>
<td>1.51 (0.60)⁺</td>
<td>15% LBPP</td>
<td>1.56 (0.50)</td>
</tr>
<tr>
<td>20% LBPP</td>
<td>1.38 (0.61)</td>
<td>20% LBPP</td>
<td>1.55 (0.42)</td>
</tr>
<tr>
<td>Comfortable Walking</td>
<td>1.52 (0.61)</td>
<td>Comfortable Walking</td>
<td>1.42 (0.46)</td>
</tr>
<tr>
<td>Fast Walking</td>
<td>2.18 (1.05)*⁺∆</td>
<td>Fast Walking</td>
<td>2.02 (0.60)*⁺∆</td>
</tr>
</tbody>
</table>

A: Peak-to-Peak (PP) heel strike knee acceleration in the medial-lateral (ML) plane during different walking conditions. * indicates significant when compared to FWB; + indicates significant when compared to 5% LBPP; ∆ indicates significant when compared to 10% LBPP. FWB – full weight-bearing; LBPP – Lower Body Positive-Pressure
### Table 6b. Medial-Lateral Knee Acceleration at Toe Off during Walking

<table>
<thead>
<tr>
<th>Affected Knee Walking Condition</th>
<th>Mean (SD)</th>
<th>Unaffected Knee Walking Condition</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FWB</td>
<td>1.97 (0.73)</td>
<td>FWB</td>
<td>2.23 (0.84)</td>
</tr>
<tr>
<td>5% LBPP</td>
<td>1.93 (0.60)</td>
<td>5% LBPP</td>
<td>2.18 (0.81)</td>
</tr>
<tr>
<td>10% LBPP</td>
<td>1.85 (0.58)</td>
<td>10% LBPP</td>
<td>2.15 (0.91)</td>
</tr>
<tr>
<td>15% LBPP</td>
<td>1.84 (0.67)</td>
<td>15% LBPP</td>
<td>1.97 (0.82)*+∆</td>
</tr>
<tr>
<td>20% LBPP</td>
<td>1.74 (0.60)*</td>
<td>20% LBPP</td>
<td>2.10 (0.91) +</td>
</tr>
<tr>
<td>Comfortable Walking</td>
<td>1.97 (0.87)</td>
<td>Comfortable Walking</td>
<td>2.18 (0.93)</td>
</tr>
<tr>
<td>Fast Walking</td>
<td>2.46 (1.08)*+∆</td>
<td>Fast Walking</td>
<td>2.73 (1.06)*+∆</td>
</tr>
</tbody>
</table>

**B**: Peak-to-Peak (PP) toe off knee acceleration in the medial-lateral (ML) plane during different walking conditions. * indicates significant when compared to FWB; + indicates significant when compared to 5% LBPP; ∆ indicates significant when compared to 10% LBPP. FWB – full weight-bearing; LBPP – Lower Body Positive-Pressure
Figure 1: The G-Trainer LBPP Treadmill

Figure 1. A subject on the G-Trainer treadmill.
**Figure 2**: Determination of the final level of unloading. The unloading protocol was used after a 5 minute warm-up, during the LBPP treadmill walking session. Accelerometry recordings and knee pain via Visual Analog Scale (VAS) were recorded every minute.
Figure 3. Wireless Tri-axial Accelerometer

Figure 3a. The wireless tri-axial accelerometer used in the study is shown.

Figure 3b. Placement of the accelerometer on the upper medial tibia with adhesive tape.
**Figure 4: Change in Knee Pain during Walking**

*Figure 4:* Mean (SE) pain as measured on the VAS during treadmill walking. Over the walking session, pain increased significantly in the FWB condition ($p = 0.002$) but not in the LBPP condition ($p = 0.58$). VAS – Visual Analog Scale; FWB – Full weight-bearing; LBPP – Lower Body Positive-Pressure. * indicates significance from pain immediately after warm-up.
Figure 5: Mean (SE) KOOS Knee Survey Scores. There was no significant difference between the 3 KOOS Knee Survey scores in any category (p > 0.05). KOOS – Knee injury and Osteoarthritis Outcome Score
There was a significant moderate negative correlation between KOOS pain score and VAS pain during walking with \( r = -0.57 \) (\( p = 0.01 \)). Higher pain scores on the VAS were indicative of lower scores recorded on the KOOS Knee Survey for pain (indicative of greater pain). VAS – Visual Analog Scale; KOOS – Knee injury and Osteoarthritis Outcome Score; FWB – full weight-bearing
Figure 7a: Proximal-Distal Change in Initial-Peak-Acceleration during Walking

Figure 7a: Mean (SE) Peak-to Peak (PP) heel strike knee acceleration decreased with LBPP in the affected knee, was lower with comfortable walkway walking, and was higher with fast walkway walking (both knees; p < 0.05). Zero on the vertical axis represents FWB. * indicates significance from FWB treadmill walking knee acceleration. IPA – Initial-Peak-Acceleration; FWB – full weight-bearing; LBPP – Lower Body Positive-Pressure; CWW – comfortable walkway walking; FWW – fast walkway walking.
Figure 7b: Proximal-Distal Knee Acceleration at Heel Strike during Walking

Figure 7b: Mean (SE) Peak-to Peak (PP) heel strike knee acceleration decreased with LBPP, was lower with comfortable walkway walking, and was higher with fast walkway walking (p < 0.05). * indicates significance from FWB treadmill walking knee acceleration. FWB – full weight-bearing; LBPP – Lower Body Positive-Pressure; CWW – comfortable walkway walking; FWW – fast walkway walking
Figure 7c: Mean (SE) Peak-to-Peak (PP) toe off acceleration decreased with LBPP, was lower with comfortable walkway walking, and was higher with fast walkway walking ($p < 0.05$). * indicates significance from FWB treadmill walking knee acceleration. FWB – full weight-bearing; LBPP – Lower Body Positive-Pressure; CWW – comfortable walkway walking; FWW – fast walkway walking.
Figure 8: Mean (SE) Peak-to-Peak heel strike acceleration during walkway walking was significantly different than treadmill walking (p < 0.05). * indicates significance from FWB treadmill walking knee acceleration. FWB – full weight-bearing; LBPP – Lower Body Positive-Pressure; CWW – comfortable walkway walking; FWW – fast walkway walking
Figure 9a: Medial-Lateral Knee Acceleration at Heel Strike during Walking

Figure 9a: Mean (SE) Peak-to-Peak heel strike acceleration during walkway walking was significantly different than treadmill walking (p < 0.05). * indicates significance from FWB treadmill walking knee acceleration. FWB – full weight-bearing; LBPP – Lower Body Positive-Pressure; CWW – comfortable walkway walking; FWW – fast walkway walking
**Figure 9b**: Mean (SE) Peak-to-Peak toe off knee acceleration decreased with LBPP (p < 0.05). Fast walking resulted in significantly greater knee acceleration all other conditions (p <0.05). * indicates significance from FWB treadmill walking knee acceleration. FWB – full weight-bearing; LBPP – Lower Body Positive-Pressure; CWW – comfortable walkway walking; FWW – fast walkway walking.
Figure 10: The Relationship between Body Weight and Knee Acceleration

Figure 10: There was a significant moderate positive relationship between body weight and proximal-distal (PD) knee acceleration at heel strike ($r = 0.50$, $p < 0.05$).
7. DISCUSSION

A thorough review of the literature indicates that these experiments are the first to assess knee pain and knee acceleration on the G-trainer anti-gravity treadmill in a symptomatic knee OA population. Overall, the objectives of the study were to: 1. Quantify the level of un-weighting that alleviated knee pain in this early-onset knee OA population; 2. Quantify knee pain associated with full weight bearing and un-weighted treadmill walking in an early-onset knee OA population; 3. Quantify parameters of knee joint acceleration during full weight bearing and un-weighted treadmill walking sessions. Our sample population consisted of fairly young, overweight but active individuals, who reported moderate to high levels of physical activity. Results indicated that a mean un-weighting of 12.3% (of body weight) resulted in significantly lower levels of knee pain as compared to full weight-bearing during treadmill walking sessions at a speed of 1.4 m/s for 25 minutes. LBPP walking also resulted in diminished knee joint pain over the duration of the walking session, as compared to full weight-bearing walking, and higher levels of unloading resulted in greater pain relief. Knee acceleration data were affected by unloading, and greater levels of unloading resulted in lower knee acceleration in all directions and in both knees. This is consistent with the current literature, which indicates that reductions in knee load occur with weight loss (Messier, et al., 2005). Finally, greater knee acceleration was seen with walkway walking than treadmill walking, which may in part be due to the treadmill itself. The attenuation of joint loads on the treadmill may serve an important purpose in rehabilitation treatments for those with knee OA.
7.1 Patient Population

Our study examined an early-onset knee OA population, with an average age of 52.9 years. This is younger than the regular age of OA onset and is representative of early-onset OA (Gelber, et al., 2000; Neuman, et al., 2008) Further, obesity increases the risk of OA and early-onset OA (Felson, 1996b), and the average BMI of our participants (33.6 kg/m^2) add to this risk. These factors show our population to be an obese and overweight early-onset knee OA population, with results that can be generalized to others in this group. Leg length and thigh girth were measured to assess the impact of abnormal differences in our study. There were no significant discrepancies between the affected and unaffected leg in leg length or thigh girth. The affected leg tended to have a smaller thigh girth, which may be due to a protective gait and favoring of the better leg by patients. However, this was not significant and may be because our population consisted of those with only mild or moderate signs of knee OA, and many of our patients had high activity levels.

Participants used a self-report scale to estimate their overall activity level during an average week over the last few months. Participants reported high levels of physical activity in all categories (light, moderate, and intense activity). The average SQUASH score of 5626 was lower than that recorded for healthy controls in the literature, which is approximately 7787 (Wendel-Vos, et al., 2003). While the SQUASH questionnaire has been deemed accurate, reliable and valid, self-report accuracy is lower for lower intensity activities (Wendel-Vos, et al., 2003), as these are often harder to remember. By contrast, our main interest was in the level of moderate and intense activity undertaken by participants, which has a high level of self-report accuracy (Wendel-Vos, et al., 2003). Our participants spent on average 15% of their time in moderate intensity activity and
12% in high intensity activity, for a total of 544 minutes per week. The Canada Physical Activity Guide recommends a minimum of 150 minutes of moderate or intense activity accumulated over the week for the average Canadian in this age group (Physiology, 2011). Our participants easily exceed this recommendation. They place a high functional demand on their joints, which makes persistent pain and the degeneration of OA an acute problem when attempting to perform daily activities in this group.

The heart rate of participants was maintained between 50-65% of heart rate maximum to ensure participants were exhibiting the same mild-moderate level of exertion. The G-trainer does not affect cardiovascular response during LBPP when up to 30% of body weight is unloaded (Hargens, et al., 1999) and in line with this, no difference in heart rate between full weight-bearing and LBPP conditions was seen in our study. This illustrates that patients can complete exercise protocols with the benefit of unloading (pain relief and knee acceleration attenuation) without a concomitant cardiovascular effect. Our participants were un-weighted to a mean level of 12.3% of body weight to minimize knee pain. This value (12% of body weight) is a realistic level of weight loss for obese/overweight patients (Christensen, et al., 2005).

7.2 Knee Pain and Function

Our population consisted of individuals with painful knee OA, and this was evident on the pain scores recorded during treadmill walking. Average pain during walking was 27.7 mm out of a possible maximum score of 100 mm. However, pain scores were highly variable between subjects, and several factors could account for this, including: differences in body weight, location of OA within the knee joint compartment, disease severity, leg mal-alignment, muscle strength, physical fitness, and psychological
factors. Pain scores on the VAS were moderately correlated with pain scores as recorded on the KOOS (r = -0.57), validating the VAS scores.

Pain was also highly variable during LBPP walking, but most patients experienced some amount of pain relief with unloading. Research has shown that greater body weight in knee OA is associated with higher knee pain, and weight loss results in pain relief (Jenkinson, et al., 2009; Messier, et al., 2004). However, in previous studies this is confounded by exercise and it is not known if the pain relief is due to weight loss or exercise. The best evidence of pain relief with the “loss” of excess weight comes from bariatric surgery studies. Most individuals undergoing this procedure report knee pain (although not necessarily related to OA), and with an average “weight loss” of 44 kg, almost all patients report a reduction or disappearance of their knee pain after surgery (Lementowski & Zelicof, 2008). Studies using unloading have had mixed results with respect to pain. Mangione et al. (1996) found highly variable pain levels and no significant trend with unloading for those with knee OA. However these individuals ambulated at a much slower speed than the current population, had a much lower average BMI (26.4 kg/m²), and the severity of OA was not recorded. Eastlack et al. (2005) used LBPP and found significant pain relief with LBPP for individuals after ACL reconstruction. This is similar to the pain relief experienced by our patients with LBPP. Further, the experience of pain relief with this technology may help to motivate those with knee OA to lose weight to further improve pain and function. Importantly, pain over the LBPP walking session was significantly lower than pain over the entire full weight-bearing walking session. This difference may allow individuals to ambulate on the treadmill, in accordance with exercise protocols in rehabilitation programs, to initiate weight loss and improve their pain and function in knee OA.
KOOS scores were reported at three time points during the study. Average KOOS scores for our population are lower than other patient population scores reported in the literature, including those that had previously suffered a serious knee injury, had ACL reconstruction or had total knee arthroplasty (Roos, et al., 1999; Roos, et al., 1998; Roos & Toksvig-Larsen, 2003). Our population scores ranked between those who were pre-TKA (lower) and pre-ACL reconstruction (higher) (Roos, et al., 1998; Roos & Toksvig-Larsen, 2003). This is lower than expected, but may be because of the method of subject selection. Subjects were self-selected respondents to media advertising, and those struggling more with their disease were more likely to respond to such advertisements. Our subjects were also overweight/obese who tend to score lower on such measures (Miller, et al., 2006). Overall there were no differences between KOOS scores from one session to the next, and this signifies that the single walking sessions did not have a measurable impact on overall function. This allows participants to approach each walking session with approximately the same level of overall function, and comparisons between walking sessions can be easily made. There was some deterioration in Function in Daily Living scores and some improvement in Quality of Life scores once individuals who did not respond to the final survey were removed from the analysis; the decline may have been due to the novel nature of the exercise or natural variation in the disease outcomes, while improvement may be due to a psychological treatment effect of walking on the G-trainer, which has been documented before (Takacs, Leiter, & Peeler, 2011).

7.3 Knee Acceleration

Our patients had similar heel strike to flat-foot accelerations in the PD direction to other knee OA patients reported in the literature (Henriksen, et al., 2008; Liikavainio, et
al., 2010; Turcot, et al., 2009). AP heel strike to flat-foot acceleration values are also similar to previous studies (Turcot, et al., 2008, 2009). ML heel strike to flat-foot acceleration values are slightly higher than those reported in the literature (Turcot, et al., 2008, 2009). This may be because half of our population experienced some type of previous knee injury, and serious knee injury tends to increase instability in the knee joint, as documented by greater ML knee accelerations in individuals who have suffered ACL tears (Yoshimura, et al., 2002). Heel strike to flat-foot will be referred to as heel strike.

A decrease in knee acceleration was seen with greater levels of LBPP in all three directions (PD, AP, ML). Research has shown that LBPP decreases loading on the knee joint (Groppo, et al., 2001; Quigley, et al., 2000), and this was confirmed by our results. However, the decrease from full weight-bearing to 5% and 10% LBPP was often not significant, and sometimes even resulted in an increase in acceleration. This may be because the level of LBPP was very small. Further, pain relief may increase knee loading through gait alterations (Schnitzer, et al., 1993; Shrader, et al., 2004), and this might have occurred with our patients when they experienced pain relief with LBPP during treadmill walking. Heel strike acceleration in the AP direction exhibited no difference with differing levels of LBPP in the affected knee. This may be because of a protective-pain mechanism – as pain relief with LBPP is experienced, the decrease in knee acceleration normally seen with LBPP is negated by the increase in knee acceleration from the removal of ‘guarding’, and a more robust gait is seen. Increasing LBPP in the ML direction resulted in a decrease in knee acceleration in the affected knee as expected, while no significant effect of LBPP was observed in the unaffected knee. This result is surprising, as LBPP was expected to result in a decrease in acceleration in both knees, as
seen in the PD direction. Variability among patients, and the limited sample size included in our study, may have obscured changes in ML knee acceleration with LBPP. Further, there may be some other mechanism at play that has not yet been fully elucidated, as a within-patient comparison of knee acceleration has not been undertaken, and the effect of unloading or weight loss on knee acceleration in the three different directions has not been analyzed.

Acceleration recorded on the walkway was also significantly different than acceleration recorded while treadmill walking. Walking at a comfortable speed on the walkway resulted in significantly lower PD and AP knee acceleration. Individuals walked at a noticeably slower pace when asked to walk comfortably, as compared to the required pace on the treadmill, and it has been demonstrated that PD acceleration increases with walking speed (Voloshin, 2000). This also corresponds with literature that shows that individuals with painful knees tend to ‘guard’ their joint against loads and exhibit a pain-protective mechanism (Henriksen, et al., 2010), resulting in lower knee loads. The relationship between OA knee pain and specific gait changes (such as knee acceleration in the three different directions) is complex and has not yet been fully elucidated.

Fast walking had significantly higher knee acceleration in all directions than comfortable walking, but also higher acceleration than treadmill walking conditions. This speed was similar to the treadmill speed, and other treadmill parameters may account for the significant difference between walkway and treadmill. The treadmill itself may help to attenuate joint loads – the belt surface is softer than other walking surfaces, and this may serve to absorb acceleration from heel strike and toe off before it reaches the knee; there is a constant residual pressure in the treadmill even when full weight-bearing, which may produce a minor lifting force; patients are secured in the treadmill and this may
reduce any accessory movement, and patients held on to the treadmill while walking, and may in this way be inadvertently creating a lifting force, adding stability to their joint and reducing acceleration. Patients were unable to complete the treadmill sessions without holding on. Muscle strength may also play a role: PD acceleration reflects force transmission across the knee and if muscles are unable to absorb force because of muscle weakness, greater acceleration may be seen. Muscle strength was not assessed in our study, but muscle weakness is known to be a common problem among those suffering from knee OA (Segal, et al., 2010). Beyond this, AP acceleration reflects AP knee stability, and a greater amount of AP acceleration may signify a greater amount of AP instability about the knee joint, which is common for those with knee OA - who often show poor proprioception (Sharma, 1999). ML acceleration is reflective of ML stability in the joint. The high rate of previous knee injury may increase ML knee instability in our population (as seen in other studies of knee injury and knee instability – (Yoshimura, et al., 2002), thereby increasing ML knee acceleration while walkway walking.

Our results are in line with those that have found no difference between OA and healthy controls during walking (Liikavainio, et al., 2010), as we saw no difference between affected and unaffected knee in our subjects. Some studies have found differences in knee acceleration between OA and healthy controls (Turcot, et al., 2008), however to our knowledge, a within-patient comparison between affected and unaffected knees has not been previously undertaken. Differences between knees may not be present, may not be as pronounced as between healthy controls and OA patients, or may be affected by pain and the OA disease itself, as mentioned above. Further, some of our patients suffered from bilateral OA, and while they did state that one knee was worse, bilateral disease or pain may cause gait changes in both knees. However, no differences
were seen when we analyzed only those with unilateral knee OA. Our patients exhibited mild to moderate levels of OA, and some gait changes are more evident in later stages of OA (Turcot, et al., 2009). Finally, there was variability between patients with respect to levels of knee acceleration. A larger sample size may help to elucidate differences that cannot be seen with the current, variable, sample.

PD knee acceleration while walkway walking was significantly correlated with body weight, as was ML knee acceleration while walkway walking. Knee loads have been correlated with body weight before (Messier, et al., 2005). When resultant acceleration (the sum of all three directions) is compared to BMI, a significant relationship emerges. The varied knee acceleration and small sample size may account for the relationship with BMI but not body weight for resultant acceleration. This relationship, however, was not seen when patients ambulated on the treadmill. This may be because other factors, such as a protective-pain mechanism, the patient’s grip of the treadmill handles or the residual pressure in the treadmill may act as a normalizing force on body weight, and may in this way obscure the relationship.

In the present study, there was little relationship between knee pain and knee acceleration parameters in any direction or walking condition. Knee pain was also not related to resultant acceleration. One possible explanation for this may be that while pain relief was significant, the absolute amount of pain relief was small. Beyond this, other factors may have a greater influence on knee acceleration including body weight, disease severity and knee alignment. Additionally, once LBPP was set and the initial accelerometry data collected, no further data were collected. As a result, the relationship between pain and knee acceleration over the entire walking session could not be examined.
7.4 Limitations

There were some limitations to the present study. Walking speed while walking on the walkway was not measured. Participants were encouraged to walk at a fast pace, similar to the fast pace on the treadmill, however, the similarity between the 2 speeds cannot be verified. Also, stride length was not measured and differences in stride length between treadmill and walkway cannot be assessed. Further, muscle strength, specifically quadriceps strength, was not assessed, and this may impact knee acceleration, as muscles play an important role in attenuating knee loads (Schipplein & Andriacchi, 1991). However, we did assess thigh girth, where large differences may be indicative of persistent deficiencies in muscle strength. We did not find any significant differences in thigh girth between affected and unaffected knees in our sample. Further, the method of leg alignment measurement, which was based on the ability of the knees or ankles to touch, may be a skewed measure to use in an obese population such as ours. While the measure used has been validated, leg alignment scores were not used in data analysis because of the possibility of invalid results. Due to the nature of the unloading protocol, the order of unloading using LBPP remained constant, with all participants un-weighted first at 5% body weight, then 10%, and so on. This may result in an interaction effect between levels of unloading; however this cannot be clarified due to the nature of the protocol. Our study was a repeated measures design, with each individual completing 2 walking sessions, an un-weighted session (condition) and a full weight-bearing session (control). While these two sessions were randomized, the effect of un-weighting may be further clarified by the introduction of a healthy population control group. Finally, the power analysis for this study indicated a sample size of 27 individuals was needed to reach 90% power. The current sample size consisted of 22 individuals, with
accelerometry data available for only 20 participants. However, the power analysis accounted for 20% attrition, and without accounting for attrition, a sample of only 22 participants was required (still maintaining a power of 90%). For this reason, we do not think our study was underpowered.

7.5 Significance and Conclusions

This investigation illustrates that LBPP technologies are an effective tool for diminishing knee joint pain and loads during walking, and may be an effective rehabilitation tool that can be used to complete exercise interventions aimed at weight loss and improvement in pain and function for those with knee OA. Key findings of our investigation included:

- A mean level of 12.3% of body weight support successfully decreased patient knee pain from full weight-bearing walking.
- Pain was significantly lower during the LBPP session as compared to the full weight-bearing treadmill walking session.
- Knee acceleration values were similar to previous values for OA patients reported in the literature.
- LBPP decreased knee acceleration in all three directions (PD, AP and ML).
- Comfortable walking on the walkway resulted in lower knee acceleration in the PD and AP direction as compared to all other conditions. This is suggestive of a ‘protective’ gait.
- All patients judged the treadmill speed to be faster than their self-selected comfortable walking speed on the walkway. This treadmill speed was similar to
their self-selected fast speed, however knee loading measured via acceleration and knee pain were significantly lower on the treadmill. This suggests the treadmill may be an appropriate environment to ambulate at lower knee accelerations.

The G-trainer treadmill may be a useful rehabilitation tool, as patients can ambulate at faster speeds with less pain and knee loading. This may allow patients with knee OA to complete exercise rehabilitation programs aimed at initiating weight loss, and improving pain and function while attenuating joint loads to reduce disease progression.

7.6 Future Directions

Studies are currently underway in our lab to assess the impact of an exercise intervention using the G-trainer on pain, function, and activity level in individuals with knee OA. Participants are completing 12 weeks of LBPP treadmill walking to examine the change in pain, function and activity level. More questions need to be answered, including:

- What is the relationship between OA disease progression and knee loading as measured by knee acceleration? Current research has looked only at certain gait variables such as gait speed, degree of knee flexion, and knee adduction moment with respect to the incidence and progression of OA (Kaufman, et al., 2001; Miyazaki, et al., 2002). Accelerometers are portable and can provide accurate real-time feedback of knee load without the need for bulky laboratory equipment. Structural progression of the disease via MRI and radiograph, and the relationship to knee load via knee acceleration, should be measured.
What is the effect of methods to reduce knee load on knee acceleration and OA disease progression? Current methods to reduce knee joint load that are being investigated include gait retraining, muscle strengthening, wedged insoles, knee bracing and weight loss; the effect of these on knee acceleration is unknown, and on disease progression over the long term is unknown.

What is the effect of different exercise interventions on knee acceleration in knee OA? The comparison of a traditional exercise program with a LBPP exercise program on knee acceleration, muscle strength, and pain levels would be of interest.

What is the effect of LBPP treadmill training on different OA populations? It is unknown if all patients with OA respond similarly to LBPP. The effect of LBPP on OA individuals with different characteristics should be considered, including overweight/obese and non-overweight populations, those with different levels of disease severity, and different age groups.

Is there a psychological effect to LBPP treadmill training? Subjective evidence from a case study (Takacs, et al., 2011) suggests that individuals may experience a heightened sense of self-efficacy after completing LBPP treadmill walking. Many of the participants in the current study also emphasized this psychological effect after treadmill walking. This may be beneficial in allowing those with knee OA to be more active and able to complete activities of daily living, but may also have a detrimental effect if individuals try to overreach their ability, and potentially engage in activities that damage their knee joint. Further research needs to be done to clarify any psychological effect of LBPP treadmill training.
8. APPENDIX

8.1 Short Questionnaire to Assess Health-Enhancing Physical Activity
Think about an average week in the past months. Please indicate how many days per week you performed the following activities, how much time on average you were engaged in this, and (if applicable) how strenuous this activity was for you?

<table>
<thead>
<tr>
<th>COMMUTING ACTIVITIES (round trip)</th>
<th>days per week</th>
<th>average time per day</th>
<th>Effort (circle please)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking to/from work or school</td>
<td>days</td>
<td>hour minutes</td>
<td>slow/moderate/fast</td>
</tr>
<tr>
<td>Bicycling to/from work or school</td>
<td>days</td>
<td>hour minutes</td>
<td>slow/moderate/fast</td>
</tr>
<tr>
<td>Not applicable</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LEISURE TIME ACTIVITIES</th>
<th>days per week</th>
<th>average time per day</th>
<th>Effort (circle please)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking</td>
<td>days</td>
<td>hour minutes</td>
<td>slow/moderate /fast</td>
</tr>
<tr>
<td>Bicycling</td>
<td>days</td>
<td>hour minutes</td>
<td>slow/moderate /fast</td>
</tr>
<tr>
<td>Gardening</td>
<td>days</td>
<td>hour minutes</td>
<td>light/moderate /intense</td>
</tr>
<tr>
<td>Odd jobs</td>
<td>days</td>
<td>hour minutes</td>
<td>light/moderate /intense</td>
</tr>
</tbody>
</table>

**Sports (please write down yourself)**
* e.g., tennis, fitness, skating, swimming, dancing

1. .................. days hour minutes light/moderate /intense
2. .................. days hour minutes light/moderate /intense
3. .................. days hour minutes light/moderate /intense
4. .................. days hour minutes light/moderate /intense
<table>
<thead>
<tr>
<th>HOUSEHOLD ACTIVITIES</th>
<th>days per week</th>
<th>average time per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light household work</td>
<td>days</td>
<td>hour minutes</td>
</tr>
<tr>
<td>(cooking, washing dishes, ironing, child care)</td>
<td>days</td>
<td>hour minutes</td>
</tr>
<tr>
<td>Intense household work</td>
<td>days</td>
<td>hour minutes</td>
</tr>
<tr>
<td>(scrubbing floor, walking with heavy shopping bags)</td>
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<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>ACTIVITY AT WORK AND SCHOOL</th>
<th>average time per week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light work</td>
<td>hour minutes</td>
</tr>
<tr>
<td>(sitting/standing with some walking, e.g., a desk job)</td>
<td>hour minutes</td>
</tr>
<tr>
<td>Intense work</td>
<td>hour minutes</td>
</tr>
<tr>
<td>(regularly lifting heavy objects at work)</td>
<td></td>
</tr>
<tr>
<td>Not applicable</td>
<td></td>
</tr>
</tbody>
</table>
8.2 Visual Analog Scale

Pain VAS

How severe is your pain?

No pain   Worst pain imaginable
8.3 Knee Injury and Osteoarthritis Outcome Score
KOOS KNEE SURVEY

Today's date: ______/_____/______ Date of birth: ______/_____/______

Name: ____________________________________________

INSTRUCTIONS: This survey asks for your view about your knee. This information will help us keep track of how you feel about your knee and how well you are able to perform your usual activities. Answer every question by ticking the appropriate box, only one box for each question. If you are unsure about how to answer a question, please give the best answer you can.

Symptoms
These questions should be answered thinking of your knee symptoms during the last week.

S1. Do you have swelling in your knee?
   - Never
   - Rarely
   - Sometimes
   - Often
   - Always

S2. Do you feel grinding, hear clicking or any other type of noise when your knee moves?
   - Never
   - Rarely
   - Sometimes
   - Often
   - Always

S3. Does your knee catch or hang up when moving?
   - Never
   - Rarely
   - Sometimes
   - Often
   - Always

S4. Can you straighten your knee fully?
   - Always
   - Often
   - Sometimes
   - Rarely
   - Never

S5. Can you bend your knee fully?
   - Always
   - Often
   - Sometimes
   - Rarely
   - Never

Stiffness
The following questions concern the amount of joint stiffness you have experienced during the last week in your knee. Stiffness is a sensation of restriction or slowness in the ease with which you move your knee joint.

S6. How severe is your knee joint stiffness after first waking in the morning?
   - None
   - Mild
   - Moderate
   - Severe
   - Extreme

S7. How severe is your knee stiffness after sitting, lying or resting later in the day?
   - None
   - Mild
   - Moderate
   - Severe
   - Extreme
Pain
P1. How often do you experience knee pain?
- Never
- Monthly
- Weekly
- Daily
- Always

What amount of knee pain have you experienced the last week during the following activities?

P2. Twisting/pivoting on your knee
- None
- Mild
- Moderate
- Severe
- Extreme

P3. Straightening knee fully
- None
- Mild
- Moderate
- Severe
- Extreme

P4. Bending knee fully
- None
- Mild
- Moderate
- Severe
- Extreme

P5. Walking on flat surface
- None
- Mild
- Moderate
- Severe
- Extreme

P6. Going up or down stairs
- None
- Mild
- Moderate
- Severe
- Extreme

P7. At night while in bed
- None
- Mild
- Moderate
- Severe
- Extreme

P8. Sitting or lying
- None
- Mild
- Moderate
- Severe
- Extreme

P9. Standing upright
- None
- Mild
- Moderate
- Severe
- Extreme

Function, daily living
The following questions concern your physical function. By this we mean your ability to move around and to look after yourself. For each of the following activities please indicate the degree of difficulty you have experienced in the last week due to your knee.

A1. Descending stairs
- None
- Mild
- Moderate
- Severe
- Extreme

A2. Ascending stairs
- None
- Mild
- Moderate
- Severe
- Extreme
For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

<table>
<thead>
<tr>
<th>Activity</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A3. Rising from sitting</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>A4. Standing</strong></td>
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<tr>
<td><strong>A5. Bending to floor/pick up an object</strong></td>
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<tr>
<td><strong>A6. Walking on flat surface</strong></td>
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<tr>
<td><strong>A7. Getting in/out of car</strong></td>
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<tr>
<td><strong>A8. Going shopping</strong></td>
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<td><strong>A9. Putting on socks/stockings</strong></td>
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<tr>
<td><strong>A10. Rising from bed</strong></td>
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<tr>
<td><strong>A11. Taking off socks/stockings</strong></td>
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<tr>
<td><strong>A12. Lying in bed (turning over, maintaining knee position)</strong></td>
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<tr>
<td><strong>A13. Getting in/out of bath</strong></td>
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<tr>
<td><strong>A14. Sitting</strong></td>
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<td></td>
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<tr>
<td><strong>A15. Getting on/off toilet</strong></td>
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</tbody>
</table>
For each of the following activities please indicate the degree of difficulty you have experienced in the last week due to your knee.

**A16. Heavy domestic duties (moving heavy boxes, scrubbing floors, etc)**

<table>
<thead>
<tr>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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<tr>
<td></td>
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</table>

**A17. Light domestic duties (cooking, dusting, etc)**

<table>
<thead>
<tr>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>

**Function, sports and recreational activities**

The following questions concern your physical function when being active on a higher level. The questions should be answered thinking of what degree of difficulty you have experienced during the last week due to your knee.

**SP1. Squatting**

<table>
<thead>
<tr>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
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</table>

**SP2. Running**

<table>
<thead>
<tr>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
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</table>

**SP3. Jumping**

<table>
<thead>
<tr>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
</tr>
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</table>

**SP4. Twisting/pivoting on your injured knee**

<table>
<thead>
<tr>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
</tr>
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<tbody>
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</table>

**SP5. Kneeling**

<table>
<thead>
<tr>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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</table>

### Quality of Life

**Q1. How often are you aware of your knee problem?**

<table>
<thead>
<tr>
<th>Never</th>
<th>Monthly</th>
<th>Weekly</th>
<th>Daily</th>
<th>Constantly</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</table>

**Q2. Have you modified your life style to avoid potentially damaging activities to your knee?**

<table>
<thead>
<tr>
<th>Not at all</th>
<th>Mildly</th>
<th>Moderately</th>
<th>Severely</th>
<th>Totally</th>
</tr>
</thead>
<tbody>
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</table>

**Q3. How much are you troubled with lack of confidence in your knee?**

<table>
<thead>
<tr>
<th>Not at all</th>
<th>Mildly</th>
<th>Moderately</th>
<th>Severely</th>
<th>Extremely</th>
</tr>
</thead>
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</table>

**Q4. In general, how much difficulty do you have with your knee?**

<table>
<thead>
<tr>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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<tbody>
<tr>
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</table>

*Thank you very much for completing all the questions in this questionnaire.*
8.4 Participant Consent Form

CONSENT TO PARTICIPATE IN RESEARCH STUDY

Title of Study: The Relationship Between Knee Pain & Body Weight in Early Onset Knee Osteoarthritis

Principal Investigator: Dr. Jason Peeler PhD., CAT(C)

Co-Investigators: Dr. Peter MacDonald MD, FRCS(C)
Dr. Jeff Leiter MSc., PhD.
Dr. Michael Davidson MD

Date: September 1, 2009

You are being asked to participate in a research study. Please take your time to review this consent form and discuss any questions you may have with the study staff. You may take your time to make your decision about participating in this study and you may discuss it with your friends, family or (if applicable) your doctor before you make your decision. This consent form may contain words that you do not understand. Please ask the study staff to explain any words or information that you do not clearly understand.

1. Purpose of the Study
This investigation will examine the relationship between knee pain & body weight in a young knee osteoarthritis (OA) population using a Lower Body Positive-Pressure (LBPP) or “anti gravity” treadmill that facilitates unloading of the body during walking. This investigation should provide researchers and clinicians with valuable information regarding the role “un-weighted” exercise could play in the rehabilitation and long term management of joint pain and deterioration associated with early onset knee OA.

2. Time Commitment
The total time commitment for your participation in the study (outside of your regularly scheduled doctor’s appointments) will be a maximum of 4 hours. This will include you participating in 2 treadmill walking sessions.

3. Procedures
For the investigation, approximately 20 participants with “x-ray” confirmed knee OA, aged 35 - 59 years, with a body mass index of greater than 25 kg/m² will be recruited. Participants will be scheduled for 2 treadmill walking sessions that occur approximately 1 week apart. During each treadmill walking session, participants will be instructed to walk at a speed of 1.4 m/s at 0° incline for a period of 25 minutes. Administration of initial intake forms, treadmill walking sessions and post treadmill questionnaires will be done by a graduate student supervised by the Study Coordinators. Participants will be asked to report on their knee pain both during and after the treadmill walking sessions. Participants will wear non-invasive accelerometers (radio transmitters) taped to the outside of their shins during walking. Prior to walking on the treadmill, participants will be asked to complete the following forms or procedures:

- Knee x-rays (radiology report to identify the stage of knee OA)
- Patient Information form
Approximately 1 week after walking on the treadmill, all participants will be asked to complete the following forms:

- KOOS Knee Survey

4. **Discomfort and Risk**
You may feel slight discomfort while walking on the treadmill, but this should be no more painful than what you experience during everyday activities such as walking.

5. **Benefits**
By participating in this study, you will be providing information to the study doctors that will allow them to better understand the role that body weight plays in causing knee pain in an osteoarthritic population. Beyond this, there may or may not be direct medical benefit to you from participating in this study.

You are not waiving any of your legal rights by signing this consent form nor releasing the investigator(s) or the sponsor(s) from their legal and professional responsibilities.

6. **Compensation**
You are participating in this study on a volunteer basis, and all clinic and professional fees, diagnostic and laboratory tests that will be performed as part of this study are provided at no cost to you. There will be no cost for the study assessment that you will receive.

7. **Confidentiality**
Information gathered in this research study may be published or presented in public forums, however your name and other identifying information will not be used or revealed. Medical records that contain your identity will be treated as confidential in accordance with the Personal Health Information Act of Manitoba. Despite efforts to keep your personal information confidential, absolute confidentiality cannot be guaranteed. Your personal information may be disclosed if required by law. All study documents related to you will bear only your assigned patient number (or code) and /or initials.

The University of Manitoba Biomedical Research Ethics Board may review research-related records for quality assurance purposes.

All records will be kept in a locked secure area and only those persons identified will have access to these records. If any of your medical/research records need to be copied to any of the above, your name and all identifying information will be removed. No information revealing any personal information such as your name, address or telephone number will leave the Pan Am Clinic.
8. **Voluntary Participation/Withdrawal from the Study**
Your decision to take part in this study is voluntary. You may refuse to participate or you may withdraw from the study at any time. Your decision not to participate or to withdraw from the study will not affect your care at this centre. If the study staff feel that it is in your best interest to withdraw you from the study, they will remove you without your consent.

We will tell you about any new information that may affect your health, welfare, or willingness to stay in this study.

9. **Medical Care for Injury Related to the Study**
In the case of injury or illness resulting from this study, necessary medical treatment will be available at no additional cost to you. If you should become physically injured as a result of any research activity, the study doctor will provide any necessary treatment, at no charge, to help you promptly recover from the injury.

You are not waiving any of your legal rights by signing this consent form nor releasing the investigator(s) their legal and professional responsibilities.

10. **Questions**
You are free to ask any questions that you may have about your treatment and your rights as a research participant. If any questions come up during or after the study or if you have a research-related injury, contact the study doctor Dr. Jason Peeler at [phone number] and/or the study coordinator Dr. Jeff Leiter at [phone number]. For questions about your rights as a research participant, you may contact The University of Manitoba, Bannatyne Campus Research Ethics Board Office at [phone number].

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

11. **Results of the Study**
All individuals who participate in this study are eligible to receive information on the outcomes of the study, via a 1 page synopsis of the key findings of the research. If you would like to receive information on the results of this study please state your mailing address below:

Address: __________________________________________________________
City: ______________________________________________________________
Postal code: _______________________________________________________
Email: ____________________________________________________________

I have read this consent form. I have had the opportunity to discuss this research study with Dr. Jason Peeler or Dr. Jeff Leiter and/or his study staff. I have had my questions answered by them in language I understand. The risks and benefits have been explained to me. I believe that I have not been unduly influenced by any study team member to participate in the research study by any statements or implied statements. Any relationship (such as employer, supervisor or family member) I may have with the study team has not affected my decision to participate. I understand that I will be given a copy of this consent form after signing it. I understand that my
participation in this study is voluntary and that I may choose to withdraw at any time. I freely agree to participate in this research study.

I understand that information regarding my personal identity will be kept confidential, but that confidentiality is not guaranteed. I authorize the inspection of any of my records that relate to this study by The University of Manitoba Research Ethics Board for quality assurance purposes.

By signing this consent form, I have not waived any of the legal rights that I have as a participant in a research study.

Participant signature___________________________ Date _____________
(day/month/year)

Participant printed name: _______________________

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given their consent

Printed Name: ________________________ Date ______________
(day/month/year)

Signature: ________________________________

Role in the study: ______________________________

Relationship to study team members:_______________________
9. REFERENCES


speed in both healthy young and older women. *Eur J Appl Physiol, 100*(3), 293-299.


