THE EFFECT OF OBESITY IN SELF-REPORTED DISABILITY, KNEE PAIN AND ISOKINETIC QUADRICEPS STRENGTH IN KNEE OSTEOARTHRITIS

by

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Abstract

Osteoarthritis (OA) of the knee is one of the most common musculoskeletal conditions resulting in disability. The incidence of knee OA increases with age and will likely increase further as the population becomes more obese and less physically active. Therefore, the objectives of this thesis were 1) to observe whether self-reported disability should be obtained before or after performance-based tests, 2) to assess changes in knee pain and observe whether symptoms of depression predict worsening of knee pain, quality of life (QoL) and increased need for surgery and, 3) to examine changes in quadriceps muscle strength and knee pain after isokinetic muscle testing.

In the first study, disability was measured using the WOMAC scores. Results indicated that all WOMAC scores were significantly higher after as compared to before the completion of performance-based tests and a physiologic test (VO₂Peak). Obese individuals with knee OA were significantly worse compared to non-obese individuals with knee OA on all WOMAC scores.

In the second study, the WOMAC pain subscale and VAS pain were significantly higher after as compared to before the completion of performance-based tests. The VAS ratings captured a significant increase in pain in both groups, but the WOMAC pain subscale only captured a significant change in the obese OA group. Depressive symptoms and BMI explained a significant proportion of variance in knee pain, quality of life and perceived need for surgery.

The third study indicated that isokinetic quadriceps muscle strength was significantly different between obese and non-obese individuals with knee OA and compared to a healthy control group at all angular velocities of 60°/s, 90°/s and 120°/s, with the obese OA group demonstrating the lowest peak torque at all angular velocities. However, it was only at 60°/s that the isokinetic peak torque showed a statistically significant difference between the obese and the non-obese groups with knee OA. Likewise, knee pain increased from before to after isokinetic muscle strength testing, but only at the angular velocity of 60°/s.
This thesis provides new information regarding the effect of obesity on self-reported disability, knee pain, depressive symptoms and quadriceps muscle strength in knee OA.
Co-Authorship

Kamary Coriolano da Silva was the primary author of all chapters within this thesis.

- Chapter 3 was co-authored by Alice Aiken, Caroline Pukall and Mark Harrison. Kamary Coriolano da Silva co-designed the study procedures with the help of Dr. Alice Aiken and was responsible for all data collection and interpretation for Chapter 3. Dr. Caroline Pukall assisted with statistical analysis. Dr. Mark Harrison assisted with radiographic readings. The manuscript was completed by Kamary Coriolano da Silva, with editing provided by the co-authors. This Chapter has been submitted for publication and is currently under review.

- Chapter 4: There were no additional co-authors beyond my main supervisor Dr. Alice Aiken and the members of my supervisory committee Dr. Caroline Pukall and Dr. Mark Harrison. Kamary Coriolano da Silva designed the study procedures with the feedback of Dr. Alice Aiken and Dr. Caroline Pukall. Kamary Coriolano da Silva was responsible for all data collection and interpretation. Chapter 4 was written by Kamary Coriolano da Silva, with editing and feedback provided by Dr. Alice Aiken, Dr. Caroline Pukall and Dr. Mark Harrison. The Manuscript that corresponds to this chapter has been submitted for publication and is currently under review.

- Chapter 5 was designed by Kamary Coriolano da Silva, with input from Dr. Alice Aiken and Dr. Mark Harrison. All data collection, analysis and interpretation for Chapter 5 were completed by Kamary Coriolano da Silva. Dr. Caroline Pukall assisted with statistical analysis. The manuscript that comprises this chapter was written by Kamary Coriolano da Silva, with editing and feedback provided by Dr. Alice Aiken and Dr. Caroline Pukall. This manuscript has been submitted for publication and is currently under review.
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MCS  Mental Component Summary

METs  Metabolic Equivalents

ml.kg/min  Millilitre-kilogram per minute

NHANES  First National Health and Nutritional Examination Survey

N.m  Newtons-metres

OA  Osteoarthritis

OARSI  Osteoarthritis Research Society International

PA  Physical Activity

PCS  Physical Component Summary

PNS  Perceived Need for Surgery

QoL  Quality of Life

SD  Standard Deviation

SF-36  Short-Form 36

BP  Bodily Pain

GH  General Health

MH  Mental Health

PF  Physical Functioning

RE  Related Emotions (emotional health problems)

RP  Role Physical

SF  Social Functioning

VT  Vitality
SPSS  Statistical Package for Social Scientists

t  Time

TKR  Total Knee Replacement

TUG  Timed Up and Go test

VAS  Visual Analog Scale

VO₂Max  Maximum Volume of Oxygen Consumption

VO₂Peak  Peak Volume of Oxygen Consumption

W  Power

WHO  World Health Organization

WOMAC  Western Ontario McMaster University Index

6 MWT  Six Minute Walking Test
Chapter 1

Introduction

1.1 Demographic and social-economic burden of osteoarthritis and obesity

Osteoarthritis (OA) is the most common chronic joint condition and may place considerable limitation on function and quality of life thereby increasing an individual’s chances of becoming disabled [1]. Approximately 3 million Canadians (1 in 10) have OA and it is estimated that 85% of Canadians will have been diagnosed with OA by the age of 70 years [2, 3]. In 2010, approximately 49% of seniors over the age of 65 years were living with symptomatic OA [4, 5]. By 2040, this number is expected to increase to 71%.

Given the lengthening of life-span, as a direct result of rising standards of living and advances in modern medicine, the prevalence of OA and its subsequent burden are projected to increase significantly [6]. Recent Canadian data on direct and indirect health care costs of OA indicate that the total health care costs of treating Canadians with OA will rise from $1.8 billion dollars in 2010 to $8.1 billion dollars in 2031[7]. And these costs may increase when obesity is taken into consideration.

The effects of OA tend to be worse in obese individuals [8, 9]. The onset of OA in weight-bearing joints such as knees and hips has been associated with obesity [10, 11]. In Canada, the 2004 Canadian Community Health Survey (CCHS) indicated that the number of obese adults was about 23.1% (over 5.5 million) of the population[12]. The results from the US First National Health and Nutrition Examination Survey (I NHANES) indicated that women with a BMI higher than 30kg/m2 but below 35kg/m2 had about 4 times the risk of developing OA compared to women whose BMI was within the recommended range (18.5–24.9 kg/m2)[13].

Obesity is commonly measured by the individual’s Body Mass Index (BMI). The standard categories for BMI include normal weight (18.5–24.9 kg/m²), overweight (25–29.9
kg/m$^2$) and obese (30 kg/m$^2$ or more)[14]. The obesity category is divided into three subcategories: class I obesity (30–34.9 kg/m$^2$), class II obesity (35–39.9 kg/m$^2$) and class III obesity (BMI ≥ 40 kg/m$^2$) [14]. Excess weight contributes significantly to a large scope of chronic diseases and is also responsible for disability, work days lost, restricted activity of daily living, and mobility limitations, thus incurring huge costs for the health care system [8, 15]. In 2001, the economic burden of obesity in Canada was estimated at $4.3 billion, representing 2.2% of the total health care costs[16].

Osteoarthritis has become one of the ten most disabling diseases worldwide [17, 18] when added to obesity, this can have a significant impact on health-related quality of life factors, including ambulation, body care and movement, emotional behaviour, home management and work, all of which contribute to the personal burden of OA associated with obesity [18-20]. Therefore, a decrease in quality of life owing to knee OA and obesity may constitute a major public health problem, and add to the cost burden of the disease.

1.2 Osteoarthritis of the Knee

The knee joint is the weight-bearing joint most commonly affected by OA [21]. Epidemiological studies estimate a prevalence of OA of 12% in people aged 25 and older and this increases to almost 68% in people aged 65 and older [22]. Since OA is a disease whose prevalence increases with age, it will become even more prevalent in the future as the bulging cohort of baby boomers grows older [23]. Joint replacement surgeries for advanced knee OA have increased considerably over the past decade. In Canada the number of total knee replacements rose by 81% in the decade from 1994-1995 to 2004-2005 [24].

OA of the knee is characterized by changes in the articular cartilage and adjacent subchondral bone and results in pain, stiffness, limitation of movement and swelling [18, 23]. The course is variable but usually there is progression to joint damage and deformities [25]. Articular
cartilage forms a thin layer lining the bony ends of all synovial joints [3]. It consists of a solid matrix (predominantly composed of collagen and proteoglycan molecules), which is saturated with water [26]. The main functions of the articular cartilage are: 1) to distribute forces during weight bearing activities, 2) to guide joint motion, 3) to maintain joint lubrication and, 4) to decrease friction between joints [27, 28]. In a healthy joint, articular cartilage may withstand the large forces associated with weight-bearing and joint motion with little or no signs of wear [28]. In unhealthy joints, the degeneration process related to OA starts as an early deterioration of the cartilage [3, 28]. Cartilage degeneration may involve fibrillation (splitting of the cartilage surface) [27]. However, not only the cartilage changes but also the periarticular bone remodels, causing osteophytes [29-31]. As the cartilage continues to wear, erosion of the subchondral bone occurs [25, 32]. Deeper into the bone structure, areas of sclerosis and cysts may form [33]. It has been acknowledged recently that other tissues are also affected in knee OA [32]. Ligaments and menisci degenerate, sometimes even before cartilage damage can be appreciated on a radiograph [32, 34]. All these may lead to increased cartilage wear and joint instability, creating a cycle of destruction. Together these joint changes ultimately cause pain, swelling and decreased range of motion of the joint, with subsequent weakness of surrounding musculature [35].

For those over the age of 65, OA of the knee accounts for greater physical disability in lower extremity tasks, such as walking, stair climbing, and rising from a chair, than any other condition [36]. Furthermore, other co-existing chronic conditions such as heart disease, pulmonary disease and particularly obesity may increase the chances of subsequent functional limitations in individuals with knee OA [12, 36]. Given the prevalence of knee OA in society and the burden of physical disability from OA, continued attention must be given to determining the most effective approaches to treat and manage painful knee OA.
1.3 Intent and structure of the thesis

This thesis aims to promote a better understanding of knee OA as it is influenced by obesity, from participants’ perspectives and biomechanical findings, based on self-reported questionnaires of disability pain, depressive symptoms and quality of life, performance-based tests and muscular testing. The intent of this thesis is to investigate whether self-reported disability should be obtained before or after performance-based tests, to explore changes in self-reported disability, the influence of depressive symptoms on knee pain and quality of life and to compare knee muscle strength in obese and non-obese individuals with knee OA.

Chapter 2 of this thesis provides a review of the current literature on obesity as a risk factor for development and progression of knee OA. It will also highlight the relevance of self-reported measures and performance-based tests to assess disability in obese and non-obese patients with knee OA, whether physical activity could be used as a predictor of disability in these populations, and whether depressive symptoms are a good indicator of increased levels of self-reported pain. Finally, it will review how knee pain and decreased quadriceps strength during muscle strength testing affects both obese and non-obese individuals with knee OA.

Chapters 3 – 5 present a series of studies of obese individuals with knee OA.

The purpose of Chapter 3 was to observe whether a self-reported disability questionnaire should be obtained before or after performance-based tests and whether self-reported disability scores obtained before and after performance-based tests differs between obese and non-obese individuals diagnosed with knee OA. Self-reported disability in individuals diagnosed with knee OA has been explored in the literature in diverse ways [37, 38]. Previous studies have used questionnaires or interviews to capture patient’s experience of their limitations on daily activities [37-39]. However, patients with knee OA tend to show physical limitations while performing daily activities such as going up or down stairs, walking long distances or standing from a sitting position [36, 40, 41]. Moreover, self-reported physical activity levels has also been used to
predict disability in different chronic conditions such as cardiovascular disease and neurological disease [42, 43], but less so for individuals diagnosed with knee OA [44, 45]. Therefore, Chapter 3 also explores whether BMI and physical activity level can predict self-reported disability in obese and non-obese individuals with knee OA.

The objectives of Chapter 4 were to observe whether self-reported pain in individuals diagnosed with knee OA would change after performance-based tests and whether self-reported pain obtained before and after performance-based tests differs between obese and non-obese individuals. In addition, depressive symptoms and BMI were used to predict worsening of knee pain, quality of life (QoL) and increased need for surgery in individuals with knee OA. Diagnosis of knee OA severity is generally made by radiographic and clinical examination [11, 46, 47]. In general, clinicians use the same methods to predict disability and pain [48, 49]. However, radiographic findings show poor correlation with knee pain [35, 49-51]. Therefore, self-reported tools developed to assess pain are important for both research and clinical use [52]. We found that excess body weight is an important factor that is associated with increased pain in individuals with knee OA [53, 54]. Likewise, depressive symptoms seem to influence the experience of pain during daily activities.

Chapter 5 explores whether quadriceps muscle strength and knee pain, assessed at different angular velocities of 60⁰/s, 90⁰/s and 120⁰/s during a single testing session, are different between obese and non-obese individuals with knee OA and whether muscle strength testing and BMI explain limited functional performance. Lower extremity muscle strength is commonly measured in knee OA research. However, the experience of pain observed during muscle strength testing has not been studied extensively in those with knee OA [55]. If an increase in knee pain is observed after functional activities, particularly activities requiring quadriceps activation, such as going up stairs or standing from a chair [36, 40, 41], these findings may suggest that quadriceps weakness is associated with knee pain.
A sample of 31 individuals diagnosed with knee OA by an orthopedic surgeon was included in this study. All 31 individuals were tested in one single session therefore; they are the same participants in Chapter 3, 4 and 5. Of the 31 participants diagnosed with knee OA, 15 were considered obese (BMI ≥ 30 kg/m\(^2\)) and 16 were non-obese (BMI ≤ 30 kg/m\(^2\)). However, in chapter 5, a sample of 15 healthy individuals without complaints of knee pain or previous injury was also examined to compare quadriceps muscle strength against obese and non-obese individuals with knee OA.

The final chapter (Chapter 6) summarizes the findings of the thesis and provides a general discussion of the studies, including recommendations and suggestions for future research.
1.4 References


Chapter 2

Literature Review

2.1 Introduction

This review will present an update on the current knowledge of obesity as a risk factor for development and progression of knee osteoarthritis (OA). It will also outline the impact of disability in obese individuals with knee OA and the importance of physical activity as a determinant factor of disability. It will discuss whether symptoms of depression suggest increased levels of self-reported pain. Finally, new findings regarding obesity and quadriceps weakness in individuals with knee OA will also be reviewed.

2.2 The link between obesity, osteoarthritis and physical inactivity

Obesity accounts for excessive body weight which may increase the load inside of the knee joints [1]. During weight-bearing activities an increased load may accelerate and promote a deterioration process of the cartilage inside the joints [2]. Longitudinal studies have demonstrated that obesity is a powerful risk factor for the development of knee OA, particularly in women [3]. Therefore, excessive body weight, as measured by Body Mass Index (BMI), may be a harmful biomechanical risk factor for the development of OA in weight-bearing joints, particularly the knee joint.

The incidence of knee OA rose 22% from 1990 to 2005 [4] and obesity incidence increased 24.1% between 2007 and 2009 [5]. A number of research studies support a well-established link between obesity and knee OA [3, 6-9]; however, it was not initially clear whether obesity directly affected the development and progression of OA or whether obesity resulted from physical inactivity due to joint pain [3]. A Framingham Study started in 1948 sought to bring light to this mystery. Investigators followed the Framingham cohort over a period of 35 years to determine the risk of knee OA based on a person’s initial
weight in 1948 [3]. They found a strong association between weight and knee OA, particularly in obese women, who had a four-fold higher incidence of knee OA than their healthy-weight counterparts [3].

Even though several studies with both males and females have found that the prevalence of knee OA tends to be greater in women than in men [2, 10, 11], it was observed that before the age of 50, the incidence of OA in most joints is higher in men than in women [3]. However, this scenario changes for those over 50, where women are more often affected with hand, foot, and knee OA than men [12].

Looking from a weight loss perspective, another study observed that overweight and obese people (BMI over 30 kg/m²) who reduce their weight by 2 kg, 5 kg or until their BMI reaches the recommended reference range would decrease their incidence of total knee arthroplasty by 10.9%, 23.6% and 57.1%, respectively [8], indicating a reduction in symptoms related to knee OA. Since sedentary life style and obesity are risk factors for knee OA [1, 15], it should be expected that differences in the prevalence of obesity in men and women accounts for the observed sex differences in knee OA.

Women also have a higher proportion of body fat to total body weight and therefore they have a higher chance of becoming obese than men [13]. In general, sex differences are related to the amount and distribution of skeletal muscle mass and fat mass, which tend to predict levels of physical functioning [14]. Owing to that, women with high fat mass and low muscle mass might experience lower levels of physical functioning than their male counterparts [14].

Today the number of younger people diagnosed with obesity is increasing, therefore onset of knee OA is now present in younger age groups of men and women than ever before [15]. Changes in society, such as work type and leisure, have affected activity and eating patterns [16]. There has been an overall shift towards less physically demanding work as well as an increased use of automated transport and passive leisure activities, such as watching television and playing video games, and this, in turn, has led to an increased number of overweight and obese people [17]. According to the World Health Organization, in 2008, more than 10% of the world’s adult population was obese [18] and consequently, these individuals are also at risk for developing knee OA over the course of a lifetime, with increasing risk as BMI rises [15].
2.3 Obesity as a risk factor for development and progression of knee osteoarthritis

Even though there is no consensus on OA’s etiologic process, the main causes of OA, with respect to obesity, include biomechanical and metabolic causes [1, 2]. These two causes have demonstrated consequences to the body’s joints, and, therefore, they have been extensively reviewed in the literature [2, 12, 19-21]. The biomechanical cause of OA due to obesity shows that the cartilage wears down as a consequence of an increased amount of weight at the joint surface [1, 2, 22], the metabolic cause of OA due to obesity also seems to show that obesity triggers the cartilage deterioration process but this process is normally observed in non-weight-bearing joints such as hands and fingers [2, 15, 19]. Both of these concepts are discussed in more detail in the following sections.

2.3.1 Obesity as a biomechanical risk factor for osteoarthritis of the knee

According to Felson et al. [12] the onset of OA may vary depending on which joint is affected. However, with respect to the knee joint, it has been observed that being overweight or obese predisposes individuals to developing OA [2, 23]. Even though healthy articular cartilage has an extensive load-support mechanism managed by its high synovial fluid, it has been observed that an increased amount of weight stresses the joint and stimulates the cartilage to wear down [1, 2]. The synovial fluid supports most of the load pressure, protecting the cartilaginous matrix from excessive stresses and therefore reduces friction at the articular surfaces [24, 25]. A recent study observed that there are mechanoreceptors at the chondrocytes, and they are very sensitive to pressure change [19]. Therefore, as the joint is constantly compressed over time, the mechanoreceptors are activated and this may stimulate the inhibition of matrix synthesis and promote cartilage deterioration [19].

The effects of the excessive load on the joint varies according to the direction of the force application and resulting motion of the joint, particularly in the knee joint [1]. The knee adduction moment, which stresses the medial compartment of the joint during dynamic activities, such as walking, is a mechanical variable associated with knee OA [26]. One study demonstrated that genu varum, in
individuals diagnosed with OA was associated with BMI (r = -0.29 and p = 0.0009); however, genu valgus was not associated with BMI [27]. Therefore, increased risk for progression of knee OA among overweight and obese persons appears to be commonly observed with varus but not valgus alignment [11, 28] and those with severe varus, rather than moderately mal-aligned limbs [27].

Several research studies have focused on exercise and weight loss treatment to decrease body weight and consequently reduce knee pain which results in significant improvements in physical function and quality of life [29-31]. Messier et al. [30] examined the effect of exercise and diet in 252 obese individuals with knee OA. The authors observed significant (p < 0.05) decrease in pain and disability in those who lost more than 5% of body weight [30]. A meta-analysis of weight loss studies suggests that at least 10% of body weight loss is needed to have a considerable clinical effect on pain and physical function [32]. Whilst many studies have focused primarily on weight loss and exercise [32-34], it is equally important to explore patients’ self-perception of disability and level of daily physical activity to set priorities to improve their quality of life while these individuals are losing weight [35, 36].

2.3.2 Obesity as a metabolic risk factor for osteoarthritis of the knee

As a metabolic risk factor, obesity may be the reason for cartilage breakdown particularly in non-weight-bearing joints such as hands and fingers [26]. Since hands are non-weight-bearing joints, the stress on hand joints experienced by obese persons does not exceed the stress felt by persons of normal weight [19, 26]. Therefore, previous studies examined the concept that overweight and obese individuals who develop OA in non-weight-bearing joints may have a systemic component that triggers cartilage breakdown and consequently leads to OA [2, 9]. More recently, adipose tissue has been considered an endocrine organ responsible for producing systemic changes that may predispose joints to cartilage deterioration [19, 20].

Cytokines, also known as adipokines, are inflammatory biomarkers typically found in individuals with OA [37]. These inflammatory biomarkers are normally released by adipose tissue and they seem to be strongly associated with OA [20, 38]. A specific adipokine called leptin, normally has a beneficial
effect on cartilage synthesis either directly, or through the upregulation of growth factors [19]. However, an excess amount of leptin may account for decreased extracellular matrix synthesis and may lead to cartilage degeneration, especially when associated with some previous injuries or excessive joint load due to obesity. [19, 39]. Surprisingly, previous studies have indicated that the level of leptin in obese people, diagnosed with knee OA, was found higher in the plasma but not in the synovial fluid, compared to non-obese people diagnosed with knee OA [20, 38]. However, another study observed a gender-specific difference [38]. The authors compared men and women with knee OA, and they observed that women exhibit higher levels of leptin in the synovial fluid, independent of body weight [38]. These findings indicate that excess body fat may trigger OA in any joint of the body. Development of OA may consequently lead to disability as a result of severe body impairment, limited activity, and restricted participation [35, 40].

Even though obesity has been shown to be responsible for increasing the development of many comorbidities, such as cardiovascular disease, gallbladder disease, hypertension and osteoarthritis [40], the idea of obesity being a disability shifts our perception of it from being only a risk factor to becoming a causal factor. In OA this is specifically due to the failure of excessive fat tissue to maintain regular lipid homeostasis, or as a result of excessive load on the joint [19, 20, 41, 42]. Therefore, obese individuals may be at increased risk of developing OA. Independent of causal mechanisms (metabolic or biomechanical), most of the symptoms of knee OA, such as stiffness, swelling and pain are disabling. And pain due to OA is the most common symptom in these individuals and unquestionably one of the most debilitating aspects of OA [43, 44].

2.4 Osteoarthritis, obesity and functional disability

Disability may be viewed as a problem residing in the affected individual or as a combination between functional impairment, participation restriction and environmental barriers that limit individuals with physical limitations from exploring their full potential [18, 45]. For example, obese individuals diagnosed with knee OA tend to experience disability due to high levels of pain which directly affect their
quality of life and level of independence [46, 47]. In addition, they indicate that the range of activities and diversity of spaces in which they can participate are limited [35].

A previous study used logistic regression to estimate the odds of dependence (need of assistance of a care giver) in 7 functional tasks and activities in elderly individuals with several chronic conditions [48]. The authors found that knee OA was among the most disabling conditions, and was associated with the most limitation in walking and climbing stairs. The adjusted percentage of disability attributable to OA was approximately 16%, and it was equal to or higher than nine other major conditions for example congestive heart failure, and chronic obstructive pulmonary disease [48]. In addition, in four out of the seven functional activities performed (walking, carrying, climbing stairs, and housekeeping) individuals with knee OA showed greater difficulties than those with other chronic conditions [48]. Another study [49] compared individuals diagnosed with knee OA with healthy control subjects. They found that persons with OA reported limitations in mobility 4.5 to 6 times more frequently than those without OA. Among those with OA, a significantly higher (p < 0.05) proportion of 61% reported limitation or restriction in mobility outside the home compared to 10.2% reported by controls. Inside the home, a significant (p < 0.05) proportion of 12.8% of those with OA reported mobility limitations compared to 2.8% of controls [49].

Obesity is not only a risk factor for OA, but it has both direct and indirect effects on the progression of functional limitations and disability [50]. For example, walking is often impaired as a direct consequence of obesity because of excess weight-bearing load on lower extremity joints [51] independent of knee OA. Other functional implications of obesity include difficulties with self-care and decreased tolerance for physical activities. Therefore, many research studies have focused on weight loss therapy and exercise as part of a regular treatment plan or as part of protocols during clinical trials [33, 52-55]; with the main objective to decrease weight and improve the quality of life and functional ability of obese and overweight individuals with knee OA. However, these studies did not target patients’ perceived disability. Even though patients’ self-report questionnaires and performance-based tests are essential to assess functional disability [56], there is no standardized recommendation emphasizing
whether measures of self-reported disability should be obtained before or after performance-based tests in individuals with knee OA. Moreover, previous studies have indicated that the individual’s experience of disability is a critical aspect of the disablement process [40, 57-59]. Therefore, an understanding of how individuals’ perceive their own level of disability is essential in order to develop better treatment plans and/or accommodate them while they lose weight and improve their health condition. The diagram represented as Figure 1 illustrates how disability may be assessed using both self-report measures and performance-based tests, yet it does not translate the sequential order in which those measurements should be obtained.

Figure 2.1: Planning increased physical activity based on the person’s perceived disability and performance-based tests followed by health care provider’s view of functional limitations.
From a clinical perspective, through knowing someone’s levels of self-reported disability and physical limitations due to OA and obesity, a trained health care professional could explore different treatment plans that include increased physical activities and exercise. Moreover, a treatment plan could accommodate each individual according to their actual capacity to exercise and consequently it could increase adherence and participation in those treatment plans.

2.4.1 The importance of self-reported measures and performance-based tests to assess disability in obese individuals with knee OA

A previous study indicated that incidence of OA increased within age groups; men between 45 and 54 years had an OA prevalence of almost 25%. As age increased to 65 to 74 years, the prevalence of OA in men was more than double at 54.6%. Similarly in women, the same initial age group had a prevalence of OA at 30.1% while the older female group experienced a doubling of this rate to 62.4% [60]. However, the incidence of obesity in the middle-age and younger individuals is growing and given the high association between obesity and knee OA, assessing both perceived disability and functional capacity of these individuals is clinically relevant [56]. Obesity, in fact, is a condition that may trigger many chronic disorders such as OA and therefore, it demands great attention and care [35, 57]. Another study observed that being obese at an average age of 37 years, the point at which OA of the knee is fairly unusual, increases the chances of developing mild knee OA at a younger age, which can progress to severe knee OA by the age of 70 [3].

As a consequence of progressive knee OA, decline in functional performance may limit persons with knee OA in remaining independent in their physical daily tasks [36, 48, 61, 62]. In addition, obese individuals tend to score poorly on performance-based tests [31, 34, 44, 63]. Therefore, previous studies [62, 64, 65] that have assessed self-reported disability scores, using measurements such as the Western Ontario McMaster University Osteoarthritis Index (WOMAC), have shown that individuals diagnosed with OA tend to have strong negative correlations with functional tests and positive correlations with both joint pain and radiographic diagnosis of knee OA. This means that their self-reported disability, which
typically shows high scores indicating increased levels of disability are well related to poor or limited functional performance. On the other hand, high disability scores are strongly related to increase in pain ratings and worsening of disease severity, based on radiographic findings. Furthermore, these studies suggested that patients’ self-report questionnaires and performance-based tests are essential to assessing functional disability [62, 64, 65]. Consequently, self-reported disability questionnaires are important tools to assess how these individuals perceive either decline or improvement in functional activities over a period of time.

Despite evidence linking obesity and knee OA to impaired physical function, there are several limitations in the current body of research. For example, the majority of studies investigating the relationship between BMI and physical function have focused on older adults and those with the highest classification of obesity (class III, BMI ≥ 40 kg/ m²) [66, 67]. Thus, little is known about the impact of BMI on physical function and development of knee OA in middle-aged adults across the broader continuum of weight ranges [3, 68].

In addition, most studies have relied solely on self-report measures to assess physical function [69-72]. A previous study stated that self-report measures should always be obtained before performance-based tests to avoid the influence that these tests may have on participant’s answers [73]. However, the authors did not justify why the influence of performance-based tests should be avoided. Notwithstanding the importance of self-report measures to assess patients’ perception of disability, a previous study indicated that performance-based tests used to assess functional performance offer a more distinct method of assessing these attributes than can be obtained by self-reports alone, and that performance measures should be viewed as core measures for people with OA of the knee and those progressing to arthroplastic surgery study [61]. If self-reported measures are obtained after performance-based tests, individuals with knee OA may report a more realistic perception of their physical limitations once they have engaged in related physical activity tasks. Moreover, self-reports of physical function represent what people experience when performing activities rather than their ability to perform activities [61, 74], which means
that after performing a physical activity, an individual may have a more realistic perception of their ability to do this activity.

Given the increased prevalence of knee OA in middle-aged adults and the disproportionate negative effect of obesity on these individuals, there is a need to more precisely define the impact of obesity and knee OA as a disabling factor in this group. It is also important to determine whether self-reported disability should be obtained before or after performance-based tests in order to obtain the most realistic picture of the person’s level of ability. Once the level of disability in these individuals is well-defined, specific treatment plans based on their actual capacity to exercise and participate in physical activities may be developed. The following sections will describe the self-report and performance-based measures used in this study.

2.4.2 Self-reported measurements of disability in knee osteoarthritis research

2.4.2.1 Western Ontario McMaster University Osteoarthritis Index (WOMAC)

The WOMAC is a disease-specific multi-dimensional, self-administered, health status instrument developed specifically for patients with lower extremity OA [75, 76]. It is widely used for evaluating effectiveness of therapeutic interventions for the treatment of OA as well as for research purposes [77]. The WOMAC consists of 24 questions aggregated into 3 sub-scales measuring: pain (5 items), stiffness (2 items), and physical function (17 items). The likert-scaled version (LK 3.1) uses mild, moderate, severe, and extreme response levels for each item. Items are rated using one of five responses (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = extreme). Three subscale scores are calculated, pain (0 to 20), stiffness (0 to 8), and physical function (0 to 68). A low total score indicates less disability, and a high total score indicates more disability [75, 78].

The WOMAC has been previously tested for reliability in different studies and clinical trials [76, 79]. The Likert Scale format of the WOMAC is widely used in research [78]. In a randomized controlled trial of 2 non-steroidal anti-inflammatory drugs among patients with knee and hip OA (N = 57), Cronbach's alphas were 0.86-0.89, 0.90-0.91, and 0.95 for the pain, stiffness, and function subscales,
respectively [76], indicating that all WOMAC subscales were highly reliable. Moreover, the WOMAC has been shown to be more responsive than other measures of knee pain [80, 81] and demonstrates good construct validity, particularly for the pain and physical function domains [76, 81]. The WOMAC is recommended by the Osteoarthritis Research Society International (OARSI) as the health status measure of choice for older adults with knee OA [56] and therefore it has been considered the gold standard for the assessment of patient-reported outcomes [82].

2.4.2.2 Self-administered Short Form-36 (SF-36) questionnaire

The SF-36 is an assessment of health related quality of life in the population and includes dimensions ranging from impairment to disability [34]. The SF-36 includes one multi-item scale that measures eight health concepts: general health (GH), vitality (VT), role physical (RP), physical functioning (PF), emotional health problems (RE), social functioning (SF), mental health (MH) and bodily pain (BP) [83-85]. The SF-36 scale ranges from 0 to 100, with higher scores indicating a better health status [83].

The SF-36 has been tested for reliability and validity. In 1996, Brazier et al. [83] tested the acceptability, validity, and reliability of the SF-36 and compared it with the Nottingham health profile, which was considered the gold standard to measure quality of life of patients with different chronic conditions [83]. The authors observed a high response rate of 83% for the SF-36 questionnaire and a high rate of completion of 95% of the health concepts. In terms of reliability, the Cronbach's alpha was greater than 0.85, reliability coefficient was greater than 0.75 for all health concepts except social functioning. In comparison with the Nottingham health profile, the SF-36 questionnaire showed a high level of reliability, which means that the SF-36 is a consistent and accurate questionnaire capable to measure general quality of life. Moreover, some patients scored zero or good health on the Nottingham health profile, while with the SF-36 the same patients were captured with low levels of poor health. To this date, the SF-36 has been used as an important addition to identify the health status of patients with different conditions [84, 86, 87].
In studies with obese patients diagnosed with knee OA, the SF-36 demonstrated that weight loss might improve physical function and general quality of life, by improving their daily level of activities, decreasing pain for example [34, 88, 89]. Therefore, the SF-36 may provide useful information particularly if associated with objective measures of function [90]. A previous study [90] investigated whether weight loss was associated with a reduction in perceived need for Total Knee Replacement surgery (TKR) due to decrease in knee pain and improvement in function. The authors observed that SF-36 sub scores PF (p ≤ .0001) and BP (p = .001) significantly increased over time. By monitoring this change, it was possible to predict need for TKR. Therefore, the use of general self-reported questionnaires such as SF-36 has been recommended during clinical assessment and for research purposes [91].

2.4.2.3 Visual Analog Scale (VAS) as a self-reported measure of pain in knee osteoarthritis

Knee pain due to OA is commonly described as one of the most debilitating aspects of OA [92, 93], therefore for elderly individuals diagnosed with knee OA, the natural process of aging combined with knee pain may account for lower levels of functional capacity [94, 95].

The VAS is a measurement tool that indicates the amount of pain an individual experiences measured across a continuum of values [96]. The scoring range is typically measured from 0 (no pain) to 10 (highest pain level). The participants are asked to grade the amount of pain they experienced by indicating it on a horizontal line between 0 and 10. The VAS has been validated for pain [97] and has been used in previous studies with patients diagnosed with OA [96, 98]. In patients with a variety of rheumatic diseases, the VAS rating has been shown to be highly correlated with a 5-point verbal descriptive scale (“nil,” “mild,” “moderate,” “severe,” and “very severe”) with correlations ranging from 0.71–0.78 [99]. This means that the experience of pain of individuals with rheumatic diseases is strongly related to VAS rating and therefore, it seems to be a useful tool to assess pain in this population. Test–retest reliability has been shown to be good, but higher among literate (r = 0.94, p < 0.001) than illiterate patients (r = 0.71, p < 0.001) before and after attending a rheumatology outpatient clinic [100].
Consequently highly educated individuals may indicate more accurately and consistently their levels of pain, compared to those with lower levels of education.

Joint pain due to knee OA is typically interpreted as a unique and subjective experience inherent to each individual [101]; Despite of its subjective interpretation, previous studies have indicated that nociceptors (peripheral sensory organs which are activated when a nociceptive stimuli cause tissue damage) may be accountable to the development of pain [102, 103]. These findings suggests that joint pain is not solely part of a subjective perception of the individuals, but a combination of impaired structures, activated during physical activities, that trigger nociceptive stimuli (causing pain) and how each individual experience the sensation of pain during activities. Consequently, the perception of knee pain may vary exponentially from one individual to another [104], on the other hand, symptomatic OA patients complain of knee pain typically after simple domestic daily activities such as going up or down stairs, walking long distances or standing from a sitting position [36, 48, 61]. Therefore knee OA is detrimental to functional activities due to an increase in pain while performing functional tasks [105]. Thus, when assessing subjects with knee OA, it seems clinically relevant to consider their perception of pain related to functional activities as a direct cause of physical limitation [105-107] and to capture the experience of pain, at the moment of its occurrence [108] as it is normally done with VAS.

2.4.2.4 Perceived Need for Surgery (PNS)

Based on a new paradigm in the health care system, called patient-centered care, health professionals should be respectful and responsive to individual patient preferences, needs, and values, and ensure that patient values guide all clinical decisions [109]. For example, from a clinical perspective it is important to empower and engage patients in the decision-making process to undergo TKR surgery. In addition, patients’ PNS could be assessed as part of clinical research protocols for those awaiting surgery, in order to evaluate their perception as part of the research goals and findings [90].

There is no standardized assessment or questionnaire to obtain patients’ PNS. Therefore, a previous study assessing changes in knee pain during weight loss therapy in women diagnosed with knee
OA, obtained patients’ PNS at baseline and at each follow up session by asking whether they still needed surgery and the answer was obtained as a yes or no response [90]. Even though it has not been studied, PNS could be assessed following the same pattern of a Visual Analog Scale tool obtained on a scale ranging from 0 to 10, 0 being no need for surgery and 10 being the highest need for surgery.

2.5 Performance-based tests and Physiological measurements of disability in knee osteoarthritis research

2.5.1 Six-Minute Walk test (6MWT)

The 6MWT is a test that measures the distance that a person can walk on a flat, hard surface in 6 minutes. The participants are allowed to stop for a short rest at any time, or stop the test completely if he/she feels necessary [110]. Therefore, the 6MWT is easy to perform and a practical test that has been used to assess exercise tolerance in patients with chronic respiratory and cardiac conditions [111]. The test has since been used as a performance-based measure of functional exercise capacity in other populations including healthy older adults, people undergoing knee or hip arthroplasty, and those with fibromyalgia and scleroderma [110, 112, 113]. The 6MWT has also been used as a one-time measure of functional status of patients, as well as a predictor of morbidity and mortality [110]. Most activities of daily living involve exertion at submaximal exercise levels, so a measure of the ability to sustain a given sub-maximal exercise is an important component of the assessment of function [113].

It may be said that performance-based tests, such as the 6MWT, used to assess function and mobility capacity, offer a more distinct method of assessing these attributes than can be obtained by self-reports alone, particularly for people with OA of the knee [61]. The ability to walk for a distance is a quick and inexpensive measure of function, and this ability is an important component of quality of life, since it reflects the capacity to undertake day-to-day activities [110].

The 6MWT has been tested for test-retest reliability [64, 110, 114]. One study [114] compared active and sedentary elderly individuals using the 6MWT. The authors found a high intraclass correlation coefficient or ICC = 0.95 when testing was done with one week apart. A high ICC indicated that elderly
individuals (sedentary or active) combined in the same group, were not similar to each other after the walking test was completed. Another study [115] examined the test-retest reliability of the 6MWT in early post-operative patients following total knee and total hip arthroplasty. They found a high ICC = 0.94 (0.88, 0.98). This time, using the 6MWT, the authors were able to indicate which group of individuals, post-operatively, had a better outcome. The 6MWT also shows good construct validity with the WOMAC (r = 0.64) and SF-36 (r = 0.69), which are considered two important subjective tools for measuring pain and function [97]. In other words, a construct validity of a test, such as 6MWT, measures what this test is intended to measure, which is the capacity to walk further distances in 6 minutes and its association with the WOMAC questionnaire and SF-36 enhance its relevance. Considering that knee OA is a disabling condition and that the 6MWT may provide an accurate assessment of these individuals’ functional level, OARSI (Osteoarthritis Research Society International) has recommended not only the 6MWT but a set of performance-based tests of physical functioning (e.g., stair-climbing test, timed up-and-go test, 6-MWT) to be used as a complementary assessment tool to self-reported measures when evaluating those with OA [56].

2.5.2 Timed Up and Go (TUG) Test

The TUG test is a test frequently used to assess balance and mobility in elderly individuals[116]. This test measures the time in seconds an individual takes to stand up from an armchair, walk a distance of 3m, turn, walk back to the chair and sit down again. Because it is fast and does not require special equipment, the TUG can be applied during a single visit [116]. The TUG is commonly used by orthopedic surgeons, physiotherapists and other healthcare professionals to assess levels of balance and mobility of individuals diagnosed with knee OA [56]. The score of the TUG test is the time required to complete the task. According to Shumway-Cook [117], the cut-off score in community-dwelling elderly subjects with high risk of falls is 14 seconds; therefore, elderly adults who took longer than 14 seconds to complete the TUG test demonstrate a higher risk for falls due to reduced balance and mobility.
More than 30% of individuals over the age of 65 years fall annually, with that number rising to 40% in subjects over the age of 80 years [117]. A previous study observed if prevalence of falls was associated with OA of the knee and lumbar spine [118]. Participants were grouped as knee OA and lumbar spondylosis based on their level OA severity, measured with Kellgren/Lawrence (K/L) scale. With regard to the knee OA group, the authors found that, the prevalence of falls in individuals with no knee OA, K/L grade 2 for knee OA, and K/L grade 3 or 4 for knee OA was 11.8%, 17.1%, and 12.5%, and 17.7%, 17.6%, and 25.6% in men and women, respectively, thus indicating that the more extensive the OA in the knee, the greater the risk of falling [118].

The TUG test correlates well with scores on the Berg Balance Scale ($r = -0.81$), gait speed ($r = -0.61$) and Barthel Index of activity of daily living ($r = -0.78$) in elderly individuals [116]. The TUG also appears to predict the patient's ability to go outside alone safely [116]. These data suggest that the TUG test is a reliable and valid test for quantifying balance and functional mobility that may also be useful for following clinical change over time. The test is quick, requires no special equipment or training, and is easily included as part of a routine physical examination [116, 119]. Therefore, the TUG is an important performance-based measure tool to evaluate mobility.

2.5.3 Stair Climbing Test

Stair climbing is an essential ability for independent ambulation and community accessibility that is described by older adults as one of the most challenging activities of daily living [120]. However, it could be even more difficult for those with limited function, such as individuals with knee OA [121]. A previous study observed if there was a distinctive characteristic in the pattern of movement during stair climbing in patients with knee OA that was associated with disease severity [122]. The authors indicated that individuals with more severe knee OA (KL ≥ 3) had greater forward trunk lean (+6.38°, $p = 0.045$) and lower knee net quadriceps moments (-35.2°, $p = 0.001$) than control subjects[122]. In more severe patients, the forward trunk lean was also correlated with a reduction in the quadriceps moment during stair climbing ($R^2 = 0.59$, $p = 0.006$) [122]. Consequently, individuals with knee OA tend to lean forward
to compensate reduced quadriceps activation during the stairs climbing. This can slow their stair ascent, and predispose them to falls.

However, stair climbing tests can also assess the functional capacity of an individual rather than just gait pattern during stair climbing. A standardized stair climbing test may be used in a clinical setting to observe whether individuals with knee OA lack the ability to do stairs independently, or to assess the degree of difficulty with stair climbing [56]. In general, a stair climbing test will require 9 to 12 steps and the individuals go to the top of the stairs as fast but as safe as they can, turn around and return back down and stop with both feet back on the ground [56]. The total time to go up and down stairs is the final outcome. Other stair climbing tests focus on muscle power output to indicate whether some individuals lack the ability to ascend stairs due to quadriceps weakness [123]. This test is a modified version from the original test proposed by Margaria et al. [124] and has been previously validated in obese individuals [125-127]. Briefly, individuals are asked to climb approximately 13 steps, as fast but as safe as possible and stop when they get to the top with both feet back on the top step [128]. Power output (W) is calculated by multiplying body weight, gravity and height in meters from the lower step to the top step and divided by the time to perform the test [128]. A higher score indicates a greater power output and consequently lower limitation to perform stairs, while the opposite would indicate lower power output and greater limitation to perform stairs.

Lafortuna et al. [123] observed if gender, age and degree of obesity affected power output during stair climbing. To assess obesity the authors used BMI and bioelectric impedance analysis (BIA) to obtain fat free mass (FFM). It was found that the power output of men, independent of age and body weight composition was significantly higher (p < 0.001) than the power output of women. Women and men older than 50 years of age showed a significant decrease (p < 0.001) in power output compared to their younger counterparts. Interestingly, FFM for both men and women was significantly (p < 0.001) more correlated to power output than BMI was for both man and women [123]. It is well-known that individuals with knee OA tend to develop quadriceps weakness and therefore many functional tasks such as stair climbing become progressively more challenging on a daily basis [44, 54]. When individuals with knee OA are
also obese they tend to perform poorly in functional tests [44], suggesting that obese individuals with knee OA would show lower power output compared to their non-obese counterparts during stair climbing tests.

2.5.4 Measurement of lower extremity muscle strength

Muscular strength may be defined as the maximum force a muscle or muscle group can generate [129]. The product of the force and the force’s moment arm (the perpendicular distance from the force’s line of action to the axis of rotation) is called torque, and is expressed in Newton-metres (N.m) [129, 130]. Dynamic strength is measured as the torque produced during concentric contraction (shortening of the muscle under load) or eccentric contraction (lengthening of the muscle under load) [129, 131]. Advances in strength testing instrumentation have led to the development of isokinetic dynamometry as an accurate method for assessing dynamic muscle strength [131].

The isokinetic measure of lower extremity muscle strength has been utilized in knee OA research and will be the focus of the next sections of this review. Advantages and disadvantages of the testing methods will also be highlighted.

2.5.4.1 Isokinetic Testing

An isokinetic dynamometer is a rotational device that consists of a lever arm attached to a dynamometer head [130]. During dynamic muscular contraction, the velocity of movement is controlled and maintained constant by the device [96, 132]. The participant applies a force on the lever arm and the resultant muscle torque is recorded through the rotation of the lever. Isokinetic dynamometers control angular velocity by providing a resistance proportional to the torque produced during muscle contraction throughout a joint’s range of motion [130, 133]. Figure 2 shows an example of a dynamometer used for clinical and research purposes.
Even though isokinetic dynamometers provide assessments of both dynamic and static muscle strength and are widely utilized in clinical and research settings, the use of isokinetic dynamometers for the measurement of muscle strength may be limited because of the disadvantages of high cost and lack of portability of the equipment [130, 134].

Angular velocity is pre-set by the examiner and kept constant by a feedback loop which continuously compares the actual angular velocity to the pre-selected velocity and adjusts the resistive moment applied by the braking mechanism of the dynamometer [130]. Isokinetic strength represents the maximum torque that can be exerted when the joint is moving at a constant, pre-set angular velocity [130, 135]. The option of concentric and/or eccentric isokinetic contractions may be selected as part of the testing protocol. Isokinetic dynamometry avoids joint or muscle overloading and is regarded as one of the safest forms of strength testing particularly for individuals with muscle or joint injury, or those recovering from joint surgery [130]. Accurate dynamic strength measurements with isokinetic dynamometry require that the effect of gravity be considered, an important factor when testing seated knee extension/flexion [130]. The performance of knee extension requires the individual to lift the weight of the limb and the
leverage of the machine against gravity, while gravity assists the motion of the limb and the lever arm during the knee flexion motion [136]. To compensate for gravity and avoid measurement errors, an automated gravity correction procedure is inherent in modern isokinetic dynamometers as part of the software system [133].

Some of the problems with isokinetic dynamometry are velocity and torque overshoot, which produce impact artifact [136, 137]. Velocity overshoot occurs at the beginning of the movement (e.g.: Knee extension or flex) when the limb accelerates past the desired velocity and braking takes place to slow the limb to the pre-selected velocity, resulting in torque overshoot (an inflated torque spike) [130, 137]. At the end of the movement range, normally during a knee flexion, when the dynamometer begins to decelerate, in anticipation of changing directions, the lever arm impacts the mechanical end stop and may oscillate slightly, producing an inflated spike [137]. These large, rapid spikes may be confused with actual muscle peak torque production and therefore those must be removed during data processing. All data must be filtered out or “windowed” to reduce the possibility of selecting incorrect peak torque values for each repetition due to end range spike oscillations and artifact in the torque curve [138]. Figure 3 shows an example of windowed data and data that is not windowed.
Optional guidelines for isokinetic testing suggest that participants must be properly positioned in the dynamometer, with the axis of rotation of the machine aligned with the joint being tested. It is also suggested to stabilize the participant with a strap to decrease motion of the limb of the joint that is being tested [130, 138].

Isokinetic tests in research trials for knee OA have focused primarily on dynamic evaluation of the quadriceps and hamstring muscles, particularly in the concentric mode. Many different angular
velocities have been tested [96, 139], but the most common angular velocities selected for isokinetic testing of the knee muscles were 60°/s, 90°/s and 120°/s [104, 138, 140, 141].

2.5.4.2 Muscle Weakness and knee pain in osteoarthritis

A stable knee joint is normally achieved in two ways, the first is the active neuromuscular control provided by muscle strength and proprioceptive sense [142], the second is the passive resistance formed by surrounding ligaments and joint capsule [143]. However, the consequent failure of one or even both systems may result in muscle weakness [96] and muscle weakness, particularly from the quadriceps muscle, has been directly associated with knee OA [96, 144]. Quadriceps muscle weakness is considered an important factor in physical disability and pain in individuals with knee OA [144]. However, it is still controversial whether muscular weakness is present in early stages of OA [96].

A previous study examined the associations of quadriceps strength and quadriceps activation with knee pain and disability in 300 individuals with knee pain [144]. Individuals with knee pain had lower voluntary quadriceps strength than those without pain (p<0.005). Quadriceps activation was also lower (p<0.005), but did not fully explain the reduction in strength [144]. The authors suggested that knee pain was strongly associated with quadriceps weakness.

The link between obesity and knee OA has been well established [3, 34, 63], however it is not clear whether quadriceps weakness is associated with obesity. Slemenda et al. [145] indicated that knee OA was associated with an increase in body weight in women (P = 0.0014) but not in men. They further reported that, among the 13 women who developed OA, there was a strong, highly significant negative correlation between body weight and extensor strength (r = -0.74, P = 0.003), meaning the higher the weight, the lower the extensor strength. On the other hand, Segal et al. [146] indicated that the quadriceps cross sectional area (CSA) did not significantly differ between BMI groups in either sex or between subjects with and without knee OA. Peak quadriceps strength also did not significantly differ by BMI group, or by the presence of knee OA, thus indicating that obesity and OA do not affect muscle strength.
Most studies have used weight loss and resistance exercise training to improve muscle strength, decrease adverse joint loading [52, 147, 148], improve function, and reduce knee pain [33, 147]. A systematic review [131] examined the effectiveness of resistance training on knee pain in patients with knee OA. Sixteen of the 18 randomized controlled trials included a supervised exercise program. Resistance training included isometric, isotonic, and isokinetic exercises. The average muscle strength improvement was 17.4%, and 56% of the studies reported a significant reduction in knee pain following resistance training [131]. However, none of these studies considered differences in muscle strength between obese and non-obese individuals with knee OA.

Therefore, further studies should explore the relationship between obesity and lower extremity muscle strength. As such, it would be important to identify whether quadriceps muscular strength differs between obese and non-obese individuals with knee OA. Moreover, quadriceps muscle weakness and knee pain are commonly reported in individuals with knee OA [104, 149], but differences in knee pain, after quadriceps strength testing, experienced by obese and non-obese individuals with knee OA are not well explained. Increased muscle strength may protect the knee from adverse loading, improve performance and decrease pain, particularly in obese individuals with knee OA [63, 150]; Therefore, from a rehabilitation perspective, conservative treatment for individuals with knee OA, who are within different BMI categories, could be better planned if potential differences in quadriceps weakness and perception of knee pain are further elucidated.

2.5.5 Submaximal oxygen consumption testing for individuals with knee OA

VO$_2$max or maximum oxygen uptake is considered the gold standard of aerobic fitness [151, 152]. It is the maximum amount of oxygen the body can consume while exercising to maximum capacity. VO$_2$max is usually standardized to body weight and expressed in milliliters of oxygen per kilogram of body weight per minute [153]. A high VO$_2$ indicates large capacity of the heart to pump blood, of the lungs to fill with larger volumes of air, and of the muscle cells to use the oxygen and remove waste
products produced during aerobic metabolism [152]. However, tests measuring VO\textsubscript{2}max are strenuous and have the potential to be dangerous in older adults since any problems with the respiratory and cardiovascular systems may be greatly exacerbated.

On the other hand, peak oxygen uptake or VO\textsubscript{2}peak is defined as the peak volume of maximal oxygen consumed per minute during an aerobic activity [154]. The VO\textsubscript{2}peak is commonly used instead of maximal aerobic capacity in adult individuals, such as untrained older subjects, who are not able to participate in strenuous activities [153, 154]. Therefore, the basic aim of such a submaximal exercise test is to determine the heart rate response to one or more work rates and uses the results to calculate the VO\textsubscript{2}peak and consequently, to predict the VO\textsubscript{2}max [152].

Different from the VO\textsubscript{2}max, to obtain the VO\textsubscript{2}peak the individual needs to get to his or her maximal heart rate, however the maximal heart rate does not need to be sustained during the exercise test [153]. Therefore, the VO\textsubscript{2}peak is safer and more comfortable to obtain than the VO\textsubscript{2}max and it is also an important component of overall health status. Oxygen consumption measured during exercise testing is directly related to cardiac output and it is affected positively by increased activity level or exercise intensity (training effect) and negatively by a sedentary life style [155].

Submaximal tests are usually used in laboratory testing to avoid the risks of an exhausting maximal work rate. Submaximal tests are usually safer to use in sedentary individuals and consequently in an older population with knee OA [44, 155]. A submaximal test may predict the level of aerobic capacity of individuals who cannot be submitted to a maximal test. The Astrand-Ryhming’s submaximal test is widely used to obtain the VO\textsubscript{2}peak in well trained individuals with a workload that may vary from 100 to 150 W on a treadmill [151]. For individuals who are physically unfit, such as untrained elderly persons with knee OA, a lower work rate of 50 W may be more adequate [44]. Moreover, cycle ergometers, rather than treadmills, may be better test modalities for submaximal testing [44, 152]. Cycle ergometers are relatively inexpensive, easily transportable and may allow blood pressure and echocardiogram to be assessed [152].
However, even submaximal exercise with lower work rates can be difficult for some individuals with knee OA [44, 156]. A treadmill or a bicycle ergometer, may aggravate pain in lower extremity joints during submaximal testing and can lead to local muscle fatigue or pain and limit performance before the capacity of the cardiovascular system is reached [44, 153, 155]. Therefore, instead of using a treadmill or a bicycle ergometer to obtain the VO$_2$peak, a previous study used an arm crank ergometer as a suitable alternative to estimate VO$_2$peak in older, obese individuals with knee OA [44]. Similarly, Helgerud et al. [153] used submaximal arm ergometer testing to estimate VO$_2$peak in older individuals with lower extremity impairments caused by vascular or neurological conditions.

The effects of the excessive load on the joint during dynamic activities, such as walking on a treadmill, or pedaling on a bicycle ergometer may stress the medial compartment of the knee increasing pain during submaximal activities [26, 44, 153]. A proposed protocol from Helgerud et al. using a crank arm ergometer [153] was previously used in a study with individuals diagnosed with hip OA [157]. Helgerud’s protocol obtained lower levels of standard errors of 11.8% and 10.7% for untrained men and women respectively compared to Astrand-Ryhming’s submaximal test [153, 154] yet, Helgerud’s protocol obtained similar levels of VO$_2$peak compared to the Astrand-Ryhming protocol [153]. A lower standard error indicates a small deviation from the actual mean of a population; in other words, the smaller the standard error, more representative the sample size will be of the overall population [158]. Helgerud et al. found no correlation between VO$_2$peak and age [153], therefore, no correction factor for age is used to predict VO$_2$peak. The main disadvantage of submaximal testing using a crank arm ergometer is that individuals usually obtain approximately 30% less of their maximal oxygen uptake compared to what they could obtain, under the same workload, if the exercise were performed with legs [159].

It is assumed that limitations in aerobic capacity may preclude individuals with knee OA or those who are obese from continuing their activities of daily living, and may manifest as a subjective sensation of fatigue [44, 152, 154]. However, the difference in levels of VO$_2$peak between obese and non-obese individuals who were diagnosed with similar severity of knee OA has not been assessed.
2.6 Radiographic measurement of osteoarthritis disease severity

Radiographic grading scales are used in clinical trials to determine the severity of knee OA and are commonly utilized as principal outcome measures to identify disease progression in longitudinal studies measuring disability and pain [160-162]. These scales assess changes in cartilage and subchondral bone and provide individual or overall grading of radiographic features [163].

The most common scale for grading knee radiographs, which has been used extensively in clinical trials, was a global scale developed by Kellgren and Lawrence (K/L) [163]. The joint is graded on a five-category scale (grades 0-4), according to the presence of osteophytes, joint space narrowing and subchondral sclerosis [163]. Global radiographic grades are as follows: grade 0, no radiographic findings of OA; grade I, possible osteophytes and doubtful narrowing of joint space; grade II, definite osteophytes and narrowing of joint space; grade III, moderate multiple osteophytes, definite narrowing of joint space and some bony sclerosis and possible deformity of bone ends; and grade IV, large osteophytes and marked narrowing of joint space, severe bony sclerosis and definite deformity of bone ends [163].

Although the K/L grading scheme is widely used, the scale is limited by its emphasis on the presence of osteophytes in the diagnosis of OA, inconsistencies in published descriptions of its radiographic features, and its relative insensitivity to change over time [164, 165]. Moreover, some patients who complain of knee pain may have worse patello-femoral OA than a typical knee OA (medial compartment of the femur and tibia) [166]. K/L does not assess patella-femoral OA [163] however, it could be modified for this purpose [166]. Therefore, it is still considered one of the best-available measures for defining the presence and degree of knee OA.

2.7 Physical activity, obesity and knee OA

Physical activity is normally defined as any form of activity or movement of the body used to expend energy [155, 167]. Engaging in physical activity not only decreases the chance of developing chronic diseases but also contributes to a better quality of life and increased participation in social activities [168, 169]. The American College of Sports Medicine (ACSM), in their guidelines for exercise
testing and prescription, in conjunction with the Center of Disease Control (CDC) [152] recommend at least 30 minutes of moderate physical activity on a daily basis. However, only 49% of the adult population in United States (US) met the CDC-ACSM physical activity recommendations [152].

On the other hand, obesity has become a global health problem of major importance [170]. In the US obesity rates increased by 37 percent between 1998 and 2006 (from 18.3 percent to 25.1 percent of the population) [171] and in Canada, the total cost in health care for obesity was about $1.6 billion, which corresponds to 2.2% of the total health care expenditures for all diseases in 2001 [17]. The Canadian Community Health Survey (CCHS) in 2004 indicated that the combined number of overweight and obese adult people was about 59.1% [13].

As the obese population increases the risk of knee OA development and progression also increase [31]. Many obese individuals who claim to have knee pain or have been diagnosed with knee OA avoid physical activities and consequently they become more physically disabled [53, 55, 172]. Therefore, self-reported physical activity should be considered an important factor to predict self-reported disability.

2.7.1 Physical activity as a predictor of disability in obese individuals with knee OA

According to the World Health Organization (WHO) [173], physical activity for adults over the age of 65 should include recreational or leisure-time physical activity such as walking or cycling activities, occupational activities (if the person is still engaged in work), household chores, play, games, sports or planned activity of at least 30 minutes of exercise daily [152]. These activities may improve cardiorespiratory and muscular fitness, bone and functional health, and reduce the risk of chronic conditions such as diabetes, heart disease, osteoarthritis, depression and cognitive decline [173, 174]. However, those over the age of 65 who are obese and diagnosed with knee OA normally avoid activities and exercise as a result of pain [33, 50, 168]. Obesity is well-known as a high risk factor for knee OA progression and development [1, 33, 34] therefore, knee pain is a typical limiting factor during daily activities [31, 61].
In addition, muscle weakness in individuals with knee OA also plays an important role as a limiting factor to engagement in physical activities [33]. Decrease in muscle strength is related to knee OA and increased levels of pain, normally observed in sedentary obese individuals [33, 63]. Considering that pain is an important factor that prevents physical activity, a previous study [175] evaluated whether quadriceps weakness, measured at angular velocity of 60°/s predicted worsening of knee pain. Participants were assessed during a follow up period of 60 months for pain using the WOMAC questionnaire. The authors indicated that lower quadriceps muscle strength at baseline was associated with an increased risk of knee pain at 60-month follow-up in obese women (P = 0.0052), but not in obese men [175]. Furthermore, muscle weakness has been reported as one of the main causes of falls in obese individuals [176] and if knee OA is present it may further increase balance issues in this population which may discourage physical activities [177].

When pain strikes, it is expected that people will avoid doing things that aggravate it. This is certainly the case for those with knee OA, many of whom tend to avoid exercise when their knee hurts. The Public Health Agency of Canada indicated that in 2007-2008, half (50%) of the general Canadian population reported being physically inactive during their leisure time [178]. The US federal Center for Disease Control and Prevention [152] revealed that approximately half of people with arthritis (53%) didn’t walk at all for exercise, and 66% stepped out for less than 90 minutes a week. Only 23% meet the current recommendation for activity of at least 30 minutes a day [152].

Walking is a great example of physical activity that can be done on a daily basis [31, 152]. A randomized clinical trial of an 18-month walking program in older adults with knee OA reduced disability and pain, and improved balance and physical performance compared to a health education control group [156]. Other studies observed that increased levels of physical activity and better diet may decrease knee pain and improve physical function [30, 90], which are important factors in patients’ decisions to undergo TKR surgery [90, 179]. One study [30] found that after 18 months of exercise and diet, obese individuals diagnosed with knee OA lost 5.7% of body weight and self-reported a significantly (p < 0.05) lower WOMAC pain score of 5.07 ± 0.47 (24% of pain improvement) and walked a significantly (p < 0.05)
longer distance of 477 meters, measured with 6 MWT, compared to their baseline results (7.27 ± 0.41 and 416.1 ± 11.3). Together these studies’ [30, 90, 156, 179] suggest that participating in physical activity and weight loss therapy are important factors in decreasing disability and improving pain, and that therefore, self-reported physical activity may be a strong predictor of self-reported disability for obese individuals diagnosed with knee OA.

Previous studies have shown that an increase in activity will progressively improve pain and function in obese individual with knee OA [31, 34] and that people will likely engage in physical activities if they believe that consequences, such as pain, will show a favorable outcome [31, 33]. However, some people simply do not know or understand the negative health cost of being obese and sedentary, and the consequences associated with knee OA [33, 50]. Consequently, it has been suggested that a reciprocal interaction of personal factors such as beliefs and values, social influence (moral support and positive pressure), and removal of physical barriers (structure and access to resources) may assist people to engage in physical activity behaviors [30, 33, 180].

In summary, decrease in physical activity due to pain, muscle weakness or fear of falling may lead to increased physical disability, suggesting that lower physical activity and self-reported disability are related [29, 31, 55, 156, 181]. A higher level of self-reported physical activity is generally used as a predictor of good health and well-being [152, 182]. While a lower self-reported physical activity has been used to predict disability in different chronic conditions such as cardiovascular disease and neurological disease [183, 184], but less so for individuals diagnosed with knee OA [172, 185]. Therefore, in order to suggest that self-reported of physical activity should be part of clinical assessments or research protocols, further studies need to examine whether self-reported physical activity is a strong indicator of disability in individuals with knee OA.
2.7.2 Measurement of physical activity - The American College of Sports Medicine (ACSM) guidelines

The literature clearly supports the importance of maintaining a good level of daily physical activity in order to decrease incidence of chronic diseases such as hypertension, type 2 diabetes, heart disease, and musculoskeletal conditions [152, 181, 186]. The ACSM guidelines for physical activity use a modified physical activity scale based on the values of Common Physical Activities (classified as Light, Moderate, and Vigorous Intensity) [152], originally reported in the *Compendium of Physical Activities: An Update of Activity Codes and MET Intensities* [174]. Physical activity can include activities that are very sedentary such as knitting or reading which can be done in a seated position, to very vigorous activities such as running, cycling or sports activities [152]. Physical activity can also be related to leisure time and job-related duties [152].

According to the ACSM guidelines, light, moderate, and vigorous intensity activity could be divided according to the amount of Metabolic Equivalents (METs) a given physical activity requires to be completed. For example: light physical activities require < 3 METs, while moderate and vigorous activities require 3 to 6 METs and > 6 METs, respectively. Three groups of daily physical activities (Walking, Household and occupation, and Leisure time and sports) were divided into three subcategories (light, moderate, and vigorous intensity activity) based on ACSM modified guidelines. For example, walking was divided into three subcategories: 1 - Light (walking slowly around the house or office: < 3 METs), 2 - Moderate (walking at 3 miles per hour or at a very brisk pace: 3 to 6 METs), and 3 - Vigorous (walking, jogging and running at 4.5 miles per hour or higher pace: > 6 METs).

2.8 Knee pain in obese individuals with knee OA

Many clinical and epidemiological studies, based on radiological information, have reported several cases of people diagnosed with severe knee OA, who indicate mild or no pain [161, 187-189], whereas others with higher levels of joint pain may not have radiographic indices of OA [190]. These findings seem to be rather conflicting, suggesting that the nature of knee pain seems to vary among
individuals diagnosed with knee OA [188, 191] and that increased levels of knee pain due to OA could be driven by a different factor rather than disease severity [192, 193].

Usually, patients diagnosed with knee OA experience increased levels of pain after simple domestic daily activities such as going up or down stairs, walking long distances or standing from a sitting position [36, 48, 61]. Therefore, performance-based tests of physical functioning have been recommended as the tests of typical activities relevant to individuals diagnosed with knee OA [61, 194]. It is well-known that knee OA is detrimental to functional activities due to a sudden increase in pain while performing functional tasks [105]. Thus, it seems clinically relevant to consider the level of pain related to functional activity as a direct cause of physical limitation [105-107]. Moreover, the increase in knee pain due to OA, has been associated with obesity [2, 8, 195, 196]. Consequently, healthcare professionals treating patients with knee OA should be aware that an increase in pain over time might be related to a significant increase in body weight [30]. Pain level experienced by OA patients is believed to be a significant contributor to reduced walking speed in patients with knee OA compared to healthy controls [197]. A previous study [198] measured pain and disability related to gait impairment in obese and overweight individuals with knee OA. The authors indicated that patients who reported more pain on the Arthritis Impact Measurement Scales (AIMS) pain subscale also walked significantly (p < 0.05) more slowly when asked to walk faster than their normal walking speed [198]. Furthermore patients who reported more pain on the WOMAC pain scale walked significantly (p < 0.05) more slowly and exhibited significantly (p < 0.001) lower peak of vertical force during the stance phase of the gait cycle [198].

However, it is not known whether change in self-reported pain experienced by obese individual with knee OA before and after performance-based tests would be similar to those who are also diagnosed with knee OA, but are not obese. Moreover, different results about level of pain are possible if assessed by different methods and captured at different moments from its occurrence [108]. The WOMAC questionnaire has been recommended as a standardized instrument used to assess self-reports of pain and disability in individuals with knee OA worldwide [75, 76]. The VAS is normally used to assess general levels of pain, but it has been previously validated in studies with individuals with knee OA [76, 100],
and therefore it is typically used in research and clinical settings [199, 200]. For example, the WOMAC is generally obtained before or a few minutes after the completion of performance-based tests [201]. While the VAS rating can be obtained before performance-based tests, it is typically obtained during or right after performance-based tests in clinical assessments [61, 199]. Taking into consideration that the experience of knee pain during a performance-based test could be momentary, it is crucial to capture the experience of pain when it occurs, as is typically measured with the VAS rating, rather than few minutes later, as measured with the WOMAC pain subscale, when some of that physical experience had receded.

Joint pain due to knee OA is viewed as a unique and subjective experience lived by the individual [101]; therefore, given the wide use of both of these measures of pain in knee OA [199] and that they may capture the experience of pain differently [90, 108], it is important to define whether one pain assessment tool would capture the experience of pain better than the other while comparing between obese and non-obese individuals with knee OA.

2.9 The effect of depressive symptoms in knee osteoarthritis pain

Depressive symptoms are commonly observed in overweight and obese individuals with OA [108]. Previous research investigating the relationship between depressive symptoms, joint pain and physical function in obese individuals with knee OA has contributed to further understanding the effect of depressive symptoms on knee pain, functional limitations and disability [93, 106, 202, 203].

Machado et al. [204] reported that the relationship between baseline pain and increased disability in individuals with knee OA is mediated by depressive symptoms. The authors indicated that during clinical assessment of individuals with knee OA, it is important to consider depressive symptoms, rather than physical limitations alone [204]. In addition they suggested that depressive symptoms and physical limitations may act as a pathway to subsequent participation restrictions and increase in pain perception [204]. Another study [205], investigated the relationship between knee pain and walking speed and the ability to rise from a chair among participants with knee pain. The authors found that high levels of depressive symptoms influenced the relationship between knee pain and functional mobility [205].
One particular study examined the relationship between depression and functional status of overweight and obese patients with knee OA. They found that levels of depression were significantly associated with the subscale scores of WOMAC function ($r = 0.54; p < 0.001$), WOMAC stiffness ($r = 0.26; p = 0.004$) and WOMAC pain ($r = 0.43; p < 0.001$) [108], indicating that increased depressive symptoms were correlated with worse WOMAC scores, or perception of disease severity. They also indicated that obese individuals with moderate to high depressive symptoms had a higher WOMAC pain score and demonstrated poorer performance in functional tests compared to obese individuals without depressive symptoms [108].

Edwards et al. [203] used depressive symptoms as predictors of greater global pain complaints before and after total knee replacement surgery. They found that after 12 months follow up, independent of successful surgical outcome, a small but significant ($p < 0.001$) number of patients continued to experience high levels of pain [203]. This finding suggested that depressive symptoms may promote enhanced pain levels, indicating that interventions intended to reduce depressive symptoms may have the potential to further improve joint replacement outcomes and patient recovery [203].

In summary, evidence suggests that depressive symptoms may have a substantial effect on perception of pain in knee OA [93, 206-208]. Even though many studies have focused on the physical aspect of disability of obese individuals with knee OA [34, 53, 63, 88, 209], the psychological aspect of the disability in this population should be equally explored, particularly if it is associated with objective measures of physical and physiological capacity. Therefore, it is important to observe whether depressive symptoms are predictive of self-reported pain. It may assist researchers and clinicians to develop clinical strategies of pain management and to accommodate patients who need treatment for knee OA and obesity while they are also being treated for depression.

2.9.1 Measuring depressive symptoms in individuals with knee OA

The Beck Depression Inventory - II (BDI-II) measures the existence and severity of symptoms of depression [210, 211]. It is a self-report measure of psychological depression that may contribute to an
understanding of the perception of disability of obese individuals with knee OA. The BDI-II is a 21-item test presented in multiple choice format, which measures the presence and degree of depression in adults [210-212]. The BDI-II is widely used as a screening instrument of depression mood for clinical research [213]. The questionnaire is composed of items relating to symptoms of depression such as hopelessness and irritability, cognition such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, weight loss, and lack of interest in sex [210, 211, 214].

Each of the 21 questions from the BDI-II questionnaire are scored on a scale value of 0 to 3. Higher total scores indicate more severe depressive symptoms. With at total possible score of 63, the standardized cut-offs used are: 0–13: minimal depression, 14–19: mild depression, 20–28: moderate depression and 29–63: severe depression. The BDI-II has been validated with the Hamilton Depression Rating Scale that has been considered as the gold standard to assess levels of depression [212, 215] and has been validated against clinical interview by a trained clinician [212]. The BDI-II is positively correlated with the Hamilton Depression Rating Scale with a correlation (r = 0.71), showing good agreement [212]. The test was also shown to have a high one-week test–retest reliability (r =0.93), suggesting that it was not overly sensitive to daily variations in mood.[211, 216] The test also has high internal consistency (α=.91) suggesting the items from BDI-II that propose to measure the same general construct produce similar scores [211].

Therefore, the use of questionnaires such as BDI-II that assess the level of depressive symptoms in individuals with chronic illness, such as knee OA, has been recommended during clinical assessment and for research purposes [202, 213].

2.10 Concluding remarks

Based on the literature presented in this chapter, the following chapters intend to further investigate the following as they relate to knee OA and obesity. Firstly, to investigate whether self-reported disability should be obtained before or after performance-based tests and to explore changes in self-reported disability (Chapter 3). Secondly, to examine whether the experience of pain in obese and
non-obese individuals with knee OA is also mediated by depressive symptoms (Chapter 4) and thirdly, how knee pain and decreased quadriceps muscle strength affect obese and non-obese individuals with knee OA in terms of functional ability (Chapter 5).
2.11 References


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3.1 Abstract

**Background:** Osteoarthritis (OA) of the knee is one of the most common musculoskeletal conditions resulting in increased levels of disability. The incidence of knee OA has increased as the population becomes more obese and consequently less physically active.

**Purpose:** The purposes of this study are three-fold: 1) To examine whether self-reported disability as measured by the WOMAC questionnaire should be obtained before or after performance-based tests. 2) To assess whether self-reported disability scores before and after performance-based tests differ between obese and non-obese individuals. 3) To observe whether physical activity and BMI predict self-reported disability before and after performance based tests.

**Methods:** The study included thirty one participants diagnosed with radiographic knee OA by an orthopedic surgeon using the Kellgren-Lawrence Scale. The sample was divided in two groups of obese individuals and non-obese individuals with knee OA. The WOMAC, used as a self-report measure of disability was obtained before and after performance-based tests.

**Results:** All WOMAC scores were significantly higher *after* as compared to before the completion of performance-based tests. This pattern of results suggested that the WOMAC questionnaire should be administered to individuals with OA *after* performance-based tests. The obese OA group was significantly different compared to the non-obese OA group on all
WOMAC scores. Physical activity and BMI explained a significant proportion of variance of self-reported disability.

**Conclusion:** Obese individuals with knee OA may over-estimate their ability to perform physical activities, and may under-estimate their level of disability compared to non-obese individuals with knee OA. In addition, body weight and self-reported physical activity seem to be strong indicators of disability in individuals with knee OA.

3.2 Introduction

The Canadian population is aging. As a result, multiple chronic health conditions and associated disabilities are expected to increase [1, 2]. Disability due to knee osteoarthritis (OA) affected approximately 4.4 million Canadians in 2010, and it is estimated that as many as 10.4 million Canadians will be diagnosed with knee OA by 2040 [3]. Given the lengthening of life-span as a direct result of rising standards of living and advances in modern medicine, the prevalence of OA and its subsequent burden are projected to increase and be higher among those over the age of 70 years [4]. In 2010, approximately 49% of seniors over the age of 70 years were living with symptomatic OA [3, 5]. By 2040, this number is expected to increase to 71%. The total direct health care cost to treat Canadians with OA in 2010 was approximately $10 billion and the total cumulative cost in direct health care expenditures in 30 years is expected to reach almost $550 billion [3].

For those over the age of 65, OA of the knee accounts for greater physical disability in lower extremity tasks, such as walking, stair climbing, and rising from a chair, than any other condition [6, 7]. Therefore, many studies have focused on patient’s functional and physical improvement and therapeutic aspects of knee OA [8-12]. Despite providing relevant contributions to the literature, these studies did not target patients’ self-reported disability. Previous studies that have assessed self-reported disability scores on measures such as the Western Ontario McMaster Osteoarthritis University Index (WOMAC) have shown that individuals diagnosed with OA tend to indicate strong negative association with functional tests and positive association with joint pain and radiographic diagnosis of knee OA [12-14]. These
studies have indicated that patients’ self-report questionnaires and functional tests are essential to assess functional disability.

According to The World Health Organization (WHO), disability is an umbrella term which covers impairment, activity limitations and participation restrictions. WHO defines each of these domains as: “Impairment is a problem in body function or structure, an activity limitation is a difficulty encountered by an individual in executing a task or action, while a participation restriction is a problem experienced by an individual in involvement in life situation” [15]. In the context of those over the age of 65 who are obese and have been diagnosed with knee OA, the damaged joint represents the problem in body function or structure, as part of the impairment domain; mobility limitations such as difficulty walking, stair climbing, and rising from a chair represents the activity domain; whereas a restriction in involvement in social/personal life situations represents participation restriction.

OA is considered to be the product of a complex interaction between systemic and local biomechanical risk factors [16, 17]. Obesity is a primary modifiable risk factor for OA and its effect includes both biomechanical and metabolic causes [18-21]. Previous researchers have found that as Body Mass Index (BMI) increases, the risk of OA in lower extremity joints also increases [16, 22, 23]. From a biomechanical point of view, excessive weight increases the load on these joints during weight-bearing activities, intensifying a deterioration process of the cartilage inside the joints, causing varying degrees of stiffness, swelling, and pain [10, 24]. Therefore, BMI is an important factor used to predict disability and worsening of many chronic conditions including osteoarthritis [25, 26]. Considering a current growth of obese individuals in our population [3], obesity may have a substantial effect on self-reported disability, particularly for those diagnosed with knee OA.

When patients report high levels of pain and self-reported disability due to knee OA, it is also expected that these individuals will have a lower rate of participation in daily physical activities [27]. A higher level of self-reported physical activity is generally used as a predictor of good health and well-being [28, 29]. However, lower self-reported physical activity has also been used to predict disability in different chronic conditions such as cardiovascular disease and neurological disease [30, 31], but less so
for individuals diagnosed with knee OA [27, 32]. Although no studies to date have used physical activity as a predictor of self-reported disability in obese individuals diagnosed with knee OA, several studies have used low impact physical activity and short term exercise as interventions to improve self-reported disability and knee pain, suggesting that physical activity and self-reported disability are related [8, 20, 33-37]. Even though physical activity and short term exercises may improve aerobic capacity, walking time, self-reported function, increase strength, decrease pain and improve physical function in patients with knee OA [9, 35], many individuals who claim to have knee pain or have been diagnosed with knee OA avoid physical activities and consequently become more physically disabled [9, 27, 34]. Therefore, self-reported physical activity should be considered an important factor to predict self-reported disability.

Even though self-reported questionnaires of disability such as the WOMAC have been traditionally used to explain disability among individuals with knee OA [38, 39], previous research has also recommended using both self-reported disability questionnaires and performance-based tests to further explore the disablement experience of individuals with knee OA [12-14, 40]. Yet, there is no standardized recommendation emphasizing whether measures of self-reported disability should be obtained before or after performance-based tests in individuals with knee OA.

The disablement experience due to a serious chronic condition may influence how individuals view themselves in terms of disability. However, the way individuals respond to their disablement experience during daily activities, depends on whether they have high or low expectations of what they are capable of doing [41]. Therefore, performance-based tests that can reproduce some activities of daily living are important tools to understand self-reported disability.

The aims of this study were three-fold: 1) To examine whether self-reported disability should be obtained before or after performance-based tests, based on whether the WOMAC score would change from before to after the completion of performance-based tests. We hypothesized that there would be an increase on the WOMAC scores of disability, pain, stiffness and function after the completion of performance-based tests. 2) To assess whether self-reported disability scores before and after performance-based tests differ between obese and non-obese individuals, and whether their self-reported
disability scores would change from before to after the completion of performance-based tests. We hypothesized that the WOMAC scores of disability, pain, stiffness and function would be higher in obese than in non-obese individuals and that only obese individuals with knee OA would show an increase on the WOMAC scores after performance-based tests. 3) To observe whether physical activity and BMI predict self-reported disability before and after performance based tests. As no other previous research has used physical activity as a predictor for self-reported disability in individuals with knee OA, no hypothesis is stated; this issue will be explored as a research question of interest.

3.3 Methods

Ethical approval was obtained from the Health Science Research Ethics Board (HSREB) of Queen’s University. Patients were recruited from the orthopedic surgical case load of one participating orthopedic surgeon at Kingston General Hospital, Kingston, Ontario, Canada. Patients were identified as potential participants for the study by the surgeon during an initial consultation. Those who showed moderate to severe radiological knee OA using the Kellgren-Lawrence Scale [42] were subsequently contacted by a research associate who described the study procedures and invited them to participate in the study once informed consent was obtained.

The patient group consisted of 31 participants between the ages of 50 and 80 years with knee OA. All participants were able to tolerate moderate activity for 60 to 90 minutes. Additionally, they were free from severe comorbidities that would prevent them from participating in the study, such as unstable angina and/or heart disease, uncontrolled blood pressure (systolic pressure > 140 mmHg, diastolic pressure > 90 mmHg) and non-knee OA related mobility restrictions (neurological and musculoskeletal). All 31 participants were eligible for the study and they were scheduled for an initial assessment conducted in a university laboratory. Participants were recruited between March 2013 and October 2013. (For specific information about recruitment, please refer to Appendix F).

Upon arrival at the laboratory, participants were given a letter of information and consent form. Upon agreement to participate, their demographic data including height and weight, responses regarding
their perceived need for surgery (PNS), data related to the functional tests, and responses to questionnaires were obtained. Disability was assessed using the Western Ontario McMaster University Osteoarthritis Index (WOMAC), see below. WOMAC scores were obtained before (Time 1) and after (Time 2) the performance-based tests of the 6 Minute Walk Test, Timed Up and Go, stair climbing test, and a submaximal aerobic test (peak of oxygen consumption or VO$_2$peak), obtained in a single visit.

3.4 Outcome Measures

3.4.1 Self-report measurements

The WOMAC questionnaire provides a total score and three subscale scores: pain, stiffness and function [12, 14]. Patients were asked to identify on a scale from 0 (none) to 4 (extreme) the degree of difficulty they have been experiencing in the past 72 hours. The pain subscale consists of 5 items with a total score ranging from 0 to 20. The function subscale consists of 17 items related to the degree of difficulty of performing activities of daily living (e.g., walking or sitting) to assess the individual’s self-reported level of physical function. Scores on this subscale range from 0 to 68. Finally, the stiffness subscale corresponds to the degree of stiffness experienced by individuals with knee OA. This section consists of 2 items (range from 0 to 8). Higher scores indicate greater pain, stiffness, and physical limitation [43]. This instrument is recommended by the Osteoarthritis Research Society International (OARSI) as the health status measure of choice for older adults with knee OA. It has been validated for use in orthopaedic and pharmacologic interventions [40, 44]

Physical activity was assessed using the physical activity scale based on the values of Common Physical Activities (classified as Light, Moderate, and Vigorous Intensity) originally reported in the *Compendium of Physical Activities: An Update of Activity Codes and MET Intensities* [45] which was summarized and modified by the American College of Sports Medicine (ACSM) in their guidelines for exercise testing and prescription [28]. The Physical Activity method described by the ACSM will be referred to as PA. According to the ACSM, light, moderate, and vigorous intensity activity could be divided according to the amount of Metabolic Equivalents (METs) a given physical activity requires to be
completed. For example: light physical activities require < 3 METs, while moderate and vigorous activities require 3 to 6 METs and > 6 METs, respectively. Three groups of daily physical activities (Walking, Household and occupation, and Leisure time and sports) were divided into three subcategories (light, moderate, and vigorous intensity activity) based on ACSM modified guidelines. For example, walking was divided into three subcategories: 1 - Light (walking slowly around the house of office: < 3 METs), 2 - Moderate (walking at 3 miles per hour or at a very brisk pace: 3 to 6 METs), and 3 - Vigorous (walking, jogging and running at 4.5 miles per hour or higher pace: > 6 METs). The participants were asked to select within each group, one subcategory that was most appropriate with his/her normal daily level of activity (figure 3.1).

**Walking**
- Walking slowly around the house/office/one block (< 3 METs)
- Walking at a very brisk pace (3 - 6 METs)
- Jogging or running, hiking at moderate pace (> 6 METs)

**Household and occupation**
- Computer work at the desk, light hand tools, light house work activities (< 3 METs)
- Heavy cleaning, washing windows, carpet cleaning, mowing lawn (3 - 6 METs)
- Shovelling snow, carrying heavy loads (bricks or wood), farming, digging (> 6 METs)

**Leisure time and sports**
- Arts & crafts, playing cards, darts, fishing, playing instruments, croquet (< 3 METs)
- Bicycling light effort, dancing (ballroom slow/fast), golf, walking, swimming (3 - 6 METs)
- Basketball game, bicycling (moderate to heavy gear), cross country skiing, soccer (> 6 METs)

**Figure 3.1: Physical Activity Questionnaire – Modified by the American College of Sports Medicine (ACSM) – Metabolic Equivalents**
Obesity is commonly measured by the individual’s Body Mass Index (BMI). The standard categories for BMI include normal weight (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²) and obese (30 kg/m² or more) [46]. The obesity category is divided into three subcategories: class I obesity (BMI 30–34.9 kg/m²), class II obesity (BMI 35–39.9 kg/m²), and class III obesity (BMI ≥ 40 kg/m²) [46].

3.4.2 Imaging examination

The Kellgren-Lawrence scale (KL) method of radiographic examination [42] was used to score the severity of knee OA and to detect differences between groups. KL is the earliest and by far the most commonly used global scale that gives an overall score of OA severity ranging from zero to four [42, 47]. The confirmation of several features were graded as an evidence of OA: grade 0, no radiographic findings of OA; grade 1, possible osteophytes and doubtful narrowing of joint space; grade 2, definite osteophytes and narrowing of joint space; grade 3, moderate multiple osteophytes and definite narrowing of joint space; and grade 4, large osteophytes and marked narrowing of joint space [42]. Both tibiofemoral compartments of the knee were assessed using a standard set of radiographs for reference [42].

3.5 Performance-based tests and physiological test

Three performance-based tests of physical functioning and one physiological test were obtained during a single testing session. The functional tests consisted of the Six Minute Walk Test (6MWT), The Timed Up and Go Test (TUG), and the modified Margaria stair climbing test [48]. Peak of oxygen consumption (VO₂peak), based on a nomogram previously used [49, 50] for calculation of upper body aerobic power from heart rate during submaximal arm cycling using an arm ergometer, was the physiological test used.

The 6MWT is generally conducted in an enclosed, quiet corridor on a 25-meter track delineated by two lines marked on the floor [51]. Patients were instructed to walk from one line to the other, covering as much ground as possible in six minutes. Individuals were told that they could rest if they became too short of breath or tired, but to continue walking when they were able to do so. To calculate
the walking distance a metre wheel was used to measure the additional steps of any incomplete lap. The procedure for the TUG requires documenting the time, in seconds, that an individual takes to rise from a standard armchair, walk 3 meters, turn, walk back to the chair and sit down [52]. The subjects were allowed to use any assistive devices that they would normally use for walking, to increase feelings of safety and comfort during the test. Prior to testing, the subjects were warned that there would be two test trials and then they were instructed about the basic sequence of the test as follows: “When I say, ‘go’, you will stand up pushing from the arm of the chair, walk to the mark (line) on the floor, turn around, walk back to the chair and sit down. I will be timing you using a stopwatch.” The subjects were allowed to rest, as much as they needed, between each trial. The average of these two trials was used as the final score. A shorter time taken to complete the task indicates a lower risk for falling and thus, greater functional status.

Lower limb mechanical power output was assessed by a stair climbing test. This test is a modified version from the original test proposed by Margaria et al. [53] and has been previously validated in obese individuals [54-56]. Participants were asked to climb one step at a time, at the highest speed possible. Even though they were allowed to use railings, participants were encouraged to use them only if they felt extremely necessary. An ordinary stair of 13 steps covering a total vertical distance of 2.0 meters was used. The final climbing time of the participants was obtained with a stop watch. The average mechanical power (W) was calculated by multiplying body mass (BM), gravity (g) and vertical distance (h) and dividing its outcome by time (t).

The arm ergometry test was used to predict the VO$_2$ peak in participants with knee OA. The participants were asked to pedal at a frequency of 70 revolutions per minute (rpm) against a constant workload of 21 Watts (125kg/min) for females and 42 Watts (250kg/min) for males. The workload was adjusted and maintained using the weights from the arm ergometer [50, 57]. To predict VO$_2$ peak using an arm cycling submaximal test, the subjects should achieve a continuous steady state heart rate either equal to or above 110 beats per minute (bpm) during the last 30 seconds of submaximal test [50]. Heart rate was monitored constantly using a chest strap heart rate monitor and a digital watch set (Polar Electro Inc., Woodbury, NY) during the test. The test’s length of time was four minutes and pulse rate was recorded.
every 10 seconds during the last 30 seconds, between the third and fourth minutes. If the difference between the lowest and the highest pulse rate, recorded in the last 30 seconds of exercising, did not exceed 5bpm, a steady state heart rate was considered to be present [49, 50]. The average HR, from the steady state, was used to find a corresponding VO₂peak (L.min) on the nomogram. VO₂peak was calculated in ml/kg/min based on the nomogram’s equation: \( VO₂peak \ (L.min) \times 1000 / Body \ Weight \ (BW) \). All of the participants reached at least 110bpm or more; consequently, a new test was not needed. However, if their heart rates had not reached at least 110bpm during the last 30 seconds of testing, the workload would have been increased by 21 W (125 kg/min) and a new test would have been initiated.

3.6 Data Analysis

Data were analyzed using the Statistical Package for the Social Sciences version 21 (SPSS 21) and Microsoft Excel 2010. The alpha (α) level was set at \( p < 0.05 \). Results are presented as mean ± standard deviation (SD) unless otherwise specified.

3.6.1 Manipulation checks and group composition analyses

Of the 31 participants diagnosed with knee OA, 15 were considered obese (BMI ≥ 30 kg/m2) and 16 were non-obese. Specifically, of the 16 non-obese participants, 9 were overweight (BMI= 25–29.9 kg/m²) and 7 were healthy weight (BMI= 18.5–24.9 kg/m²). A one-way ANOVA between overweight and healthy weight participants with knee OA demonstrated that they did not differ significantly on any demographic or main variables of interest, including radiographic examination findings (p’s > .05). Likewise, a chi-square analysis did not reveal any significant difference in gender (p > .05) between the overweight and healthy weight groups. Therefore, we combined the overweight and healthy weight groups into one group: the non-obese OA group. Radiographic examination was obtained from all 31 participants diagnosed with knee OA. A one-way ANOVA between the obese OA and non-obese OA groups was conducted to examine whether knee OA severity was significantly different between these
two groups. The analysis indicated no significant differences between groups on knee OA severity (p > .05). Please find baseline information of both groups on table 3.1.

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<th>Mean (SD)</th>
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<th>Maximum</th>
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<tr>
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<td>62.1</td>
<td>24.4</td>
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<tr>
<td>Obese OA</td>
<td>104.3 (19)</td>
<td>70</td>
<td>143.7</td>
<td>28.8</td>
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<tr>
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<td>62</td>
<td>82</td>
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<tr>
<td>Obese OA</td>
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<td>4.0</td>
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<tr>
<td>Non-obese OA</td>
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<td>2.0</td>
<td>4.0</td>
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<td>PA</td>
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<td>5.0</td>
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<tr>
<td>Non-obese OA</td>
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<td>4.0</td>
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<tr>
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<td>79.95</td>
<td>344.00</td>
<td>30.5</td>
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</tr>
<tr>
<td>Non-obese OA</td>
<td>328 (114.6)</td>
<td>170.00</td>
<td>579.75</td>
<td></td>
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<tr>
<td>VO2 Peak</td>
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<tr>
<td>Obese OA</td>
<td>15.6 (5.3)</td>
<td>8.36</td>
<td>28.47</td>
<td>18.4</td>
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<td>14.28</td>
<td>36.56</td>
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<td>TUG</td>
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<tr>
<td>Obese OA</td>
<td>11.0 (2.8)</td>
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<td>18.94</td>
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<tr>
<td>Obese OA</td>
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<td>75.0</td>
<td>425.0</td>
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<td>0.000</td>
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<td>447.7 (65.6)</td>
<td>325.0</td>
<td>555.0</td>
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</tr>
</tbody>
</table>

Table 3.1: (SD) Standard deviation; x – Ray (Kellgren – Lawrence or KL); Age (yrs.); BMI (kg/m²); Body Weight (Kg); PA: physical Activity– Metabolic Equivalents (METs); Stair Climbing - Lower limb mechanical power- Watts (W); Six Minute Walking Test (6MWT) – meters (m); Timed Up and Go Test (TUG) – seconds (s); Peak of oxygen consumption (VO2peak) – (ml.kg/min). Obese OA (N = 15) and Non-obese OA (N= 16). All significant values between groups were (p ≤ .0001)

Further analyses between obese OA and non-obese OA groups indicated that body weight (F (1, 29) = 24.4; p ≤ .0001) and BMI (F (1, 29) = 28.8; p ≤ .0001) were significantly different between groups (table 3.1). Analyses indicated that PA (F (1, 29) = 41.6; p ≤ .0001) was significantly different between
groups (table 3.1). The three performance-based tests (stairs climbing, 6MWT, and TUG) and the VO_{2} peak (physiological test) were also compared between obese OA and non-obese OA groups. Analyses indicated that results from the stairs climbing test (F (1, 29) = 21.3; p ≤ .0001), 6MWT (F (1, 29) = 30.5; p ≤ .0001), TUG (F (1, 29) = 18.4; p ≤ .0001) and the VO_{2} peak (F (1, 29) = 30.5; p ≤ .0001) were significantly different between groups (table 3.1).

3.7 Results

In order to test our first hypothesis that self-reported disability should be obtained after performance-based tests because there would be an increase in the WOMAC scores of disability, pain, stiffness and function after performance-based tests, four repeated measures ANOVA were conducted. The repeated measures ANOVA examined whether the WOMAC total scores of disability, pain, stiffness, and function of all 31 participants changed from before (Time 1) to after (Time 2) performance-based tests (figure 3.2). Results indicated that the WOMAC total scores of disability significantly changed (F (1, 30) = 10.9; p = .002) from Time 1 (mean = 41, SD = 13.3) to Time 2 (mean = 50.2, SD = 20.4). The WOMAC pain scores also changed significantly (F (1, 30) = 7.1; p = .012) from Time 1 (mean = 8.3, SD = 3.2) to Time 2 (mean = 9.7, SD = 4.6). In addition, the WOMAC stiffness scores changed significantly (F (1, 30) = 5.2; p = .022) from Time 1 (mean = 4.3, SD = 1.7) to Time 2 (mean = 4.9, SD = 1.9). Finally, the WOMAC function scores changed significantly (F (1, 30) = 10.3; p = .003) from Time 1 (mean = 29.4, SD = 9.6) to Time 2 (mean = 35.4, SD = 14.4) (figure 3.2).
In order to test our second hypothesis that the WOMAC scores of disability, pain, stiffness, and function would be higher in obese than in non-obese individuals and that only obese individuals with knee OA would show an increase in the WOMAC scores after performance-based tests, four additional repeated measures ANOVA were conducted. The repeated measures ANOVA examined whether the obese OA group had higher scores of WOMAC total disability, pain, stiffness, and function as compared to the non-obese OA group (figure 3.3). The results indicated that the WOMAC total score (F (1, 29) = 31.7; p < .0001) and the WOMAC pain (F (1, 29) = 24; p < .0001), stiffness (F (1, 29) = 14; p = .001), and function (F (1, 29) = 31.6; p < .0001) subscale scores were significantly different between groups, with the obese OA group demonstrating higher WOMAC total (mean = 57.5), pain (mean = 11.5), stiffness (mean = 5.5) and mobility (mean = 40.5) scores as compared with the non-obese OA group (total: mean = 35.1, pain: mean = 6.6, stiffness: mean = 3.7, mobility: mean = 24.7). The within-groups factor examined whether the mean scores of each group changed after performance-based tests were completed. Results indicated that only the obese OA group changed significantly from Time 1 to Time 2.
on all WOMAC scores: WOMAC total (Time 1 mean = 48.4 and Time 2 mean = 66.6; F (1, 29) = 21.2 p < .0001), pain (means = 9.33 and 13.3; F (1, 29) = 12; p = .002), stiffness (means = 5.0 and 6.1; F (1, 29) = 7.2; p = .012), and mobility (means = 34.0 and 47.0; F (1, 29) = 19; p < .0001). No significant changes in mean values were observed in the non-obese OA group from Time 1 to Time 2 (figure 3.3).

In order to test our exploratory question as to whether physical activity and BMI would predict WOMAC scores of disability, pain, stiffness, and function, we conducted a stepwise regression analyses between the WOMAC scores and BMI and PA. Prior to the analyses, we ensured that there was no evidence of strong multicollinearity among the independent variables (all Pearson correlation coefficients (r) were < 0.80) [58]. Two initial stepwise regression analyses were conducted to explore whether BMI

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**Figure 3.3: Repeated Measures ANOVA - WOMAC scores before (Time 1) and after (Time 2) performance-based tests. Groups: Obese OA (N=15) and Non-obese OA (N= 16). P ≤ 0.001 (between groups) and P < 0.05 (within groups – obese OA only)**
and PA would predict the WOMAC total score before (Time 1) and after (Time 2) the completion of performance-based tests. At Time 1, the regression analysis indicated that PA alone explained a significant proportion of variance of the WOMAC total, $R^2 = 30\%$, $F (1, 29) = 11.8; p = .002$. Remarkably, at Time 2, PA and BMI explained a significant proportion of variance of the WOMAC total, $R^2 = 60\%$, $F (1, 29) = 20.1; p < .0001$. This finding indicates that after performance-based tests, BMI and physical activity accounted for 60% of variance in participants’ self-reported disability. Given that there were significant levels of association between the WOMAC total score and physical activity and BMI, we then conducted six stepwise regressions between WOMAC subscale scores (pain, stiffness, and function) and BMI and PA at Time 1 and Time 2 (table 3.2).

| WOMAC total | Time 1: PA alone explained a significant proportion of variance of the WOMAC total, $R^2 = 30\%$, $F (1, 29) = 11.8; p = .002$
| Time 2: PA and BMI explained a significant proportion of variance of the WOMAC total, $R^2 = 60\%$, $F (1, 29) = 20.1; p < .0001$
| WOMAC pain | Time 1: BMI alone explained a significant proportion of variance of the WOMAC pain, $R^2 = 16.3\%$, $F (1, 29) = 5.6; p = .024$
| Time 2: PA alone explained a significant proportion of variance of the WOMAC pain, $R^2 = 37\%$, $F (1, 29) = 17.4; p < .0001$
| WOMAC stiffness | Time 1: BMI alone explained a significant proportion of variance of the WOMAC stiffness, $R^2 = 17.3\%$, $F (1, 29) = 6.0; p = .020$
| Time 2: BMI alone explained a significant proportion of variance of the WOMAC stiffness, $R^2 = 32\%$, $F (1, 29) = 13.6; p = .001$
| WOMAC function | Time 1: PA explained a significant proportion of variance of the WOMAC function, $R^2 = 32\%$, $F (1, 29) = 13.9; p = .001$
| Time 2: PA and BMI explained a significant proportion of variance of the WOMAC function, $R^2 = 63.7\%$, $F (1, 29) = 24.6; p < .0001$

Table 3.2: Summary table of Stepwise regression analysis—Physical Activity and BMI were predictors of disability
At Time 1, the stepwise regression analysis indicated that the BMI alone significantly (F (1, 29) = 5.6; p = .024) explained $R^2 = 16.3\%$ of the variance in the WOMAC pain subscale score. However, at Time 2, the PA alone significantly (F (1, 29) = 17.4; p < .0001) explained $R^2 = 37\%$ of the WOMAC pain subscale score variance (table 3.2). These results indicate that BMI accounted for just over 16\% of the variance in self-reported knee pain at Time 1, while at Time 2 PA accounted for 37\% of the variance in self-reported knee pain.

Stepwise regression analysis indicated that at Time 1 BMI explained a significant proportion of variance of the WOMAC stiffness subscale scores $R^2 = 17.3\%$, F (1, 29) = 6.0; p = .020). Likewise, at Time 2, BMI explained a significant proportion of variance of the WOMAC stiffness subscale scores $R^2 = 32\%$, F (1, 29) = 13.6; p = .001) (table 3.2). These findings suggest that at Time 1, BMI accounted for just over 17\% of the variance in self-reported stiffness in the knee joint, while at Time 2, BMI accounted for 32\% of the variance in self-reported stiffness.

Stepwise regression analyses indicated that PA alone explained a significant proportion of variance of the WOMAC function subscale score, $R^2 = 32\%$, F (1, 29) = 13.9; p = .001) at Time 1. At Time 2, BMI and PA explained a significant proportion of the variance of the WOMAC function subscale score, $R^2 = 63.7\%$, F (1, 29) = 24.6; p < .0001) (table 3.2). These results indicate that PA accounted for 32\% of variance in participants’ self-reported functional limitation at Time 1, but at Time 2, the combination of PA and BMI accounted for 63.7\% of variance in participants’ self-reported functional limitation.

3.8 Discussion

The results of the current study demonstrated that all WOMAC scores were significantly higher after as compared to before the completion of performance-based tests. This pattern of results suggests that measures of self-reported disability, when possible, should be administered to individuals with OA after performance-based tests (figure 3.2) because it captures participants’ experience of physical limitations in real time. Further analyses indicated significant differences between the obese OA and non-
obese OA groups on all WOMAC scores, with the obese OA group demonstrating higher scores for disability (figure 3.3). In addition, when comparing the groups, the non-obese OA group did not show any significant change in WOMAC scores from Time 1 to Time 2, whereas all scores from the obese OA group changed significantly from Time 1 to Time 2 (figure 3.3). Finally, we observed that physical activity and BMI explained a significant proportion of variance of self-reported disability, particularly after performance-based tests were completed. These results indicate that physical activity and BMI accounted for greater variability in self-reported disability scores from individuals with knee OA (table 3.2).

3.8.1 Increase in WOMAC scores after performance-based tests in individuals with knee OA

As reported in previous studies, individuals with higher severity of knee OA tend to indicate higher WOMAC scores of disability [13, 35]. A review study indicated that WOMAC total scores ranging from 23 to 33 or higher than 33 are suggestive of high disability levels [59]. When clustered as one group we observed that our participants had an average score of 41 for the WOMAC total before performance-based tests. This number increased significantly (p = .002) to 50.2 after performance-based tests (figure 3.2). The increase of the WOMAC total score suggests that our participants had a more realistic perception of their physical limitations once they engaged in related physical activity tasks, suggesting that relying on self-reported disability alone may lead to an overestimation of one’s abilities. Even though the conclusion from a previous study stated that self-report measures should always be obtained before performance-based tests to avoid the influence that these tests may have on participant’s answers [60], the authors did not justify why the influence of performance-based tests should be avoided. OARSI (Osteoarthritis Research Society International), on the other hand, has recommended that a set of performance-based tests of physical functioning (e.g., stair-climbing test, timed up-and-go test, 6-MWT) be used as a complementary assessment tool to self-reported measures [40]. Yet, there is no standardized
recommendation emphasizing whether measures of self-reported disability should be obtained before or after performance-based tests in individuals with knee OA.

Larsson and Mattsson [61] obtained a fair to good correlation (r = 0.56) between self-reported disability and functional limitations in obese women and in a normal-weight control group. Yet, the authors found that neither severely obese nor older women self-reported more disability than less obese and younger ones, suggesting that relying on self-report alone is not ideal. This finding supports our idea that self-report questionnaires may be more reliable if the questionnaires are administered after performance-based tests are completed. This way, an answer for a simple question such as “how difficult do you think it is to complete a task”, may be different if the same question is asked after someone actually completes the given task.

In a study with 93 patients awaiting total hip or knee replacement, Stratford et al. [13] argued that performance-based tests of physical functioning based on time alone inadequately represents the breadth of health concepts associated with functional status. The authors correlated a self-report measure (the Lower Extremity Functional Scale, LEFS) with the summed score of three performance-based functioning scores (self-paced walk, timed up-and-go, and stair test) to increase reliability. Then they separately correlated the LEFS with the 40-meter fast self-paced walk test. They found that the correlation of the LEFS with the summed timed performance-based tests scores was not higher than the correlations of the LEFS with the 40-meter fast self-paced walk. By adding pain scores and exertion scores into the model, the correlation between performance-based tests and self-reported physical functioning increased. Therefore, they considered this as evidence for a lack of content validity of the performance-based test of physical functioning. On the other hand, Terwee et al. [62] indicated that self-report measures of physical functioning are more influenced by the amount of pain experienced than performance-based tests of physical functioning. In fact, Terwee et al. [62] indicated that the study from Stratford et al. [13] is evidence for a lack of content validity of self-report measures, not performance-based tests. Terwee et al. [62] observed that, correlations between (two) self-reported measures of functioning (WOMAC and SF-
and (two) pain measures were higher \( (r = 0.57 \text{ and } r = 0.74) \) than correlations between performance-based tests of functioning and the two pain measures \( (r = 0.20 \text{ and } r = 0.26) \) [62].

Apart from the studies mentioned above, another study [63] indicated that performance-based tests used to assess joint pain and function offer a more distinct method of assessing these attributes than can be obtained by self-reports alone and that performance measures should be viewed as core measures for people with OA of the hip or knee and those progressing to arthroplasty. Self-reports of physical function, on the other hand, represent what people experience when performing activities rather than their ability to perform activities [63, 64]. Therefore, extrapolating from the authors’ conclusion and based on our results (figure 3.2), we suggest that if self-report measures are to be obtained during a clinical assessment, it should be obtained after performance-based tests are completed.

3.8.2 Change in WOMAC scores in obese and non-obese individuals after performance-based tests

Even though individuals with knee OA tend to report higher levels of disability [4, 13], we noticed in our study that only the obese OA group reported a significant increase on WOMAC scores from before to after performance-based tests (figure 3.3). No changes in self-reported disability score were observed in the non-obese OA group following performance-based tests. According to Terwee et al. [62], self-report measures of physical functioning are more influenced by the amount of pain experienced than performance-based measures of physical functioning. Our obese OA group reported higher levels of pain, based on the WOMAC score, before and after performance-based tests (figure 3.3). Therefore, we suggest that obese individuals with knee OA tend to underestimate their level of disability until a higher level of pain is triggered; consequently, for these individuals, performance-based tests should be completed prior to self-reported measures of disability.

It has been well documented that obese individuals diagnosed with knee OA tend to score poorly on performance-based tests of physical functioning and that they have higher levels of pain [8, 35, 65, 66]. A previous study [65] compared obese control subjects with obese individual diagnosed with knee
OA. Results indicated that VO₂peak was significantly higher in obese controls (mean = 1.58 ± 0.23 L/Kg) compared to obese individuals with knee OA (mean = 0.98 ± 0.20 L/Kg). The authors also found that obese control subjects walked for significantly longer distances (p < 0.001) compared with their counterparts with knee OA. Unfortunately, the authors did not indicate the total walking distance from both obese groups and did not use a healthy weight group to compare with the obese control group. Even though the obese control group performed better during the walking test, walking is often impaired as a direct consequence of obesity through excess weight-bearing [67]. Obesity is also a major risk factor for knee OA development [18, 19]. Therefore, the ability to participate in physical activity and exercise seems to be worse in obese individuals with knee OA, but not necessarily better in obese individuals without knee pain. Yet, recent studies emphasize that physical activity and exercise are essential to decrease pain and attenuate progression of knee OA particularly in obese individuals [20, 35, 68]. Our results indicated that the obese OA group had a significant increase in disability scores before and after performance-based tests, and that compared to the non-obese OA group, their performance-based tests were significantly lower, including the walking test and VO₂Peak (table 3.1).

Verbrugge and Jette [41, 69] speculated that perception of disability due to serious chronic conditions makes a great difference in the disablement experience and therefore influences how individuals view themselves in terms of disability, and whether the individuals have high or low expectations during their daily activities. Similar to our study findings, knee pain in the non-obese OA group, who have higher levels of physical activity, may cause some decrease in walking ability and therefore, it might be seen as a limiting factor in daily activities. On the other hand, other individuals diagnosed with knee OA who are obese had already adapted to walking short distances, and may not have rated their self-report disability in walking very high. Yet, we found that the obese individuals with knee OA will likely give a more accurate rating of their self-report disability when they find themselves exposed to a situation where their physical and functional capacities are tested in real-time.
3.8.3 Physical activity and knee OA

Studies using diet and exercise as part of an intervention to decrease disability in individuals with knee OA indicated that after losing weight and engaging in moderate levels of physical activity, obese individuals seem to improve on their levels of function and knee pain [8, 20, 35, 70]. One particular study [70], found that after 18 months of exercise and diet followed by 5.7% of body weight loss, an obese group diagnosed with knee OA self-reported a significantly (p < 0.05) lower WOMAC pain score of 5.07 ± 0.47 (24% of pain improvement) and walked a significantly (p < 0.05) longer distance of 477 meters, measured with 6 MWT, compared to their baseline results (7.27 ± 0.41 and 416.1 ± 11.3). Even though the previous study [70] used diet and exercise to improve disability levels, and we did not, we may extrapolate from their findings to compare to our findings. Compared to our obese OA group, who participated in low levels of daily physical activity, the WOMAC pain scores were 9.8 before and 13.2 after performance tests and the walking distance was 270 ± 109.4 meters. Compared to our non-obese OA group, who participate in moderate levels of daily physical activity, their obese group still did slightly better after 18 months of diet and exercise. Our non-obese OA group self-reported scores of 6.8 before and 6.5 after performance-based tests on the WOMAC pain and the walking distance was 447.7 meters. Even though the findings from this previous study suggested that weight loss therapy and exercise are important to decrease disability in individuals with OA [70], their findings also support our results by suggesting that participating in exercise or increasing the amount of physical activity is also an important factor in decreasing disability and improving pain. Consequently physical activity may be a strong predictor of self-reported disability for obese individuals diagnosed with knee OA.

Our results indicated that physical activity and BMI explained a significant proportion of variance of self-reported disability, as measured by the WOMAC (table 3.2). We also observed that individuals with lower levels of daily physical activity (obese OA group), were likely to indicate higher levels of self-reported disability, joint pain, stiffness and lower function before and particularly after performance-based tests (figure 3.3). A recent study [71] observed that vigorous, but not moderate, physical activity was found to be associated with 1.35 times greater risk for worsening cartilage lesions (increase in
disability). Another study [72], indicated that low levels and higher levels of physical activity are strongly related to progression of knee OA, based on structural damage of the cartilage. The authors indicated that those who walked either less than 8103 or more than 10580 steps per day had significantly higher odds of middle cartilage worsening compared to those who walked between 8126 and 10580 steps per day [72].

Our obese OA group self-reported low levels of daily physical activity (3.3 METs) which was significantly lower (p < .0001) compared to the non-obese OA group, who self-reported moderate levels of daily physical activity (5.7 METs). Interestingly, only our obese OA group showed an increased change in self-reported disability scores after performance-based tests. Therefore, in agreement with the abovementioned studies [71, 72], moderate levels of physical activity rather than low levels of physical activity may be beneficial to reduce the progression of knee OA. Considering that low levels of physical activity may not stimulate the beneficial metabolic activity to decrease knee OA progression, moderate levels of physical activity may be the ideal level of physical activity that can contribute to decreased self-reported disability in these individuals [73]. Consequently, according to our results and supported by recent scientific findings we may suggest that self-reported physical activity is a strong predictor of disability particularly for those individuals with low levels of physical activity (obese OA group).

Despite some limitations such as difficulty to recruit patients within a BMI category of 18.5-24.9 kg/m² during consultation with an orthopedic surgeon and lack of external funding to intensify recruiting and consequently increasing sample size, we obtained important findings of significant impact and relevance to clinical setting. Future studies should include a larger sample, a longitudinal design, and variables such as weight loss and varying levels of physical activity in the view to developing a series of physical activities and related exercises suitable for individuals with knee OA. A study such as this one would provide additional information on long-term changes in self-reported disability and performance-based tests. Further investigations are needed to determine whether change in self-reported disability is consistent over time and if so, to observe whether such change in perception would support patient’s adherence in weight loss treatment.
In conclusion, self-reported disability scores of obese individuals diagnosed with knee OA were significantly worse after they completed performance-based tests. Obese individuals with knee OA may over-estimate their ability to perform physical activities, and may under-estimate their level of disability compared to non-obese individuals with knee OA. In addition, self-reported physical activity seems to be a strong indicator of disability in individuals with knee OA, particularly for individuals with a sedentary life style. The findings of this study suggest that especially for obese individuals with knee OA, performance-based tests should be included in any assessment of disability, and specifically these tests should be completed prior to self-reported measures of disability.
3.9 References


Chapter 4

Change in knee pain after performance-based tests in obese and non-obese individuals diagnosed with osteoarthritis of knee

*Manuscript Under Review, Journal of Obesity, June 2014*

4.1 Abstract

**Background:** Joint pain is a debilitating aspect of knee osteoarthritis (OA) and obese individuals with knee OA tend to be more susceptible to pain and consequently limited functional performance.

**Objectives:** 1) to examine whether self-reported pain, measured with the WOMAC pain subscale and VAS pain ratings, of individuals diagnosed with knee OA would change after performance-based tests were completed 2) to assess whether self-reported pain before and after performance-based tests differs between obese and non-obese individuals 3) to observe whether depressive symptoms and BMI are predictive of self-reported pain before and after performance based tests, and predictive of QoL and PNS at baseline.

**Methods:** The study included thirty one participants diagnosed with radiographic knee OA by an orthopedic surgeon using the Kellgren-Lawrence Scale. The sample was divided in two groups of obese individuals with knee OA and non-obese individuals with knee OA. Two self-reported measures, the WOMAC and VAS assessed knee pain before and after performance-based tests in these two groups of individuals. In addition, QoL and PNS.

**Results:** The WOMAC pain subscale and VAS ratings were significantly higher after as compared to before the completion of performance-based tests for all study participants. When participants were further sub-divided into obese and non-obese groups, the obese group
demonstrated significantly higher levels of self-reported pain. The VAS ratings showed a significant increase in pain in both groups from Time 1 to Time 2, but the WOMAC pain subscale only captured a significant change in the obese OA group after completion of performance-based tests. Depressive symptoms and BMI explained a significant proportion of variance in VAS ratings, but depressive symptoms alone explained a significant proportion of variance in the WOMAC pain subscale scores. A significant proportion of variance in quality of life and perceived need for surgery were also explained by depressive symptoms and BMI.

**Conclusion:** The VAS pain rating may be a better tool for assessing knee pain of obese and non-obese individuals diagnosed with knee OA right after performance-based tests, because it captures the pain at the moment of its occurrence. Furthermore, symptoms of depression might predict decreased quality of life, increase in knee pain and perceived need for surgery in obese individuals. Therefore, treatment of depression and a successful weight loss management may be necessary to improve the lifestyle of some individuals with knee OA.

### 4.2 Introduction

Osteoarthritis (OA) is a significant cause of joint pain and disability in elderly individuals [1] and joint pain is unquestionably one of the most debilitating aspects of OA [2, 3]. OA is heterogeneous and characterized by progressive cartilage loss, deterioration of subchondral bone, osteophyte formation and synovial inflammation, resulting in joint pain. Previous studies have suggested that mechanical factors such as obesity [4-7], limb malalignment and knee injury [8-11] are risk factors for knee OA progression and the consequent increase in knee pain. Whilst the disease progression may cause pain and increase disability, approximately 50% of persons with structural change consistent with OA are asymptomatic [12]. Therefore, the nature of knee pain and its causes seem to vary among individuals diagnosed with knee OA [1, 13].

In general, radiological information is used during a clinical consultation to identify the severity level of knee OA and consequently, disability and pain [12, 14]. However, the confirmation of
radiological OA is not necessarily an indication of symptomatic knee OA [15, 16]. Symptomatic knee OA, which is clinically more important, requires consistent presence of joint pain on most of the days of the previous month [12, 17]. Some clinical and epidemiological studies have reported several cases of people with structural change, based on radiological information, who indicate mild or no pain [1, 12, 18, 19], whereas others with higher levels of joint pain may not have severe radiographic indices of OA [16]. Therefore, radiographic imaging of the knee OA seems to be an invaluable tool for the assessment and diagnosis of disease severity [20], but not joint pain. Joint pain due to knee OA is interpreted as a unique and subjective experience lived by the individual [21]; therefore, self-reported tools developed to assess pain are important for both research and clinical use [22].

The Western Ontario McMaster University Osteoarthritis Index (WOMAC) is a validated questionnaire used to assess self-reported disability in individuals with knee OA [23, 24]. It has been used extensively in clinical trials with individuals with knee OA [6, 7, 25]. The WOMAC consists of three subscales that assess pain, stiffness and function [26]. Although the WOMAC also yields a total score in addition to the subscale scores, subscale scores have been reported in the literature independently of the total score [27]. The WOMAC pain subscale has been consistently used to assess pain, and change in pain—particularly at its chronic stage [4]—in individuals with knee OA [26]. However, self-reported pain may show different results if captured at the moment of its occurrence [28]. Pain intensity can also be assessed using a visual analog scale (VAS) during a clinical evaluation or right after a functional test that triggers pain [29, 30]. The VAS is a validated pain measurement tool that has been used to assess pain levels of individuals with knee OA [22]. Given the use of both of these measures in knee OA [30] and that they may capture the experience of pain differently [4, 28], it may be appropriate to use both generic (VAS) and specific (WOMAC) tools [30] and observe whether one measure would capture the experience of pain better than the other.

Typically, symptomatic OA patients complain of knee pain after simple domestic daily activities such as going up or down stairs, walking long distances or standing from a sitting position [29, 31, 32]. Therefore, performance-based tests of physical functioning, such as the stair-climbing test, the timed up-
and-go test and the 6 Minute Walk Test (6MWT), have been recommended as the tests of typical activities relevant to individuals diagnosed with knee OA [29, 33]. It is well-known that knee OA is detrimental to functional activities due to a sudden increase in pain while performing functional tasks [34]. Thus, it seems clinically relevant to consider the level of pain related to functional activity as a direct cause of physical limitation [22, 34, 35].

Moreover, considering the current increase of obese individuals in our population [36], obesity may have a substantial effect on self-reported pain, particularly for those diagnosed with knee OA. Excessive body weight is an important factor that contributes to increased pain in individuals with knee OA [5, 37]. Weight gain may affect the knee joint via changes to the biomechanical components of gait [38], including the external knee adduction moment [38, 39] which determines the load distribution on the medial compartment of the knee [40]. A study demonstrated that OA severity in individuals with genu varum was associated with BMI (r = -0.29 and p = 0.0009) [38]. A recent study suggested that for every kilogram gained, WOMAC pain scores went up by 1.9 points on a 500-point scale, the WOMAC stiffness scores worsened by 1.4 points (on a 200 point scale), and the WOMAC function scores increased by 6.1 points (on a 1,700 point scale) [2]. It is likely that obese and non-obese individuals with knee OA are somehow exposed to similar daily physical tasks, such as stair climbing, walking, and standing from a sitting position; however, it is not known whether self-reported pain experienced by obese individual with knee OA before and after performance-based tests would be similar to those who are also diagnosed with knee OA, but are not obese.

Another factor that seems to influence self-reported pain is depressive symptoms [41]. A previous study that observed the relationship between depressive symptoms and knee pain indicated that the presence of depressive symptoms limits the ability to associate knee pain complaints to radiographic OA. In other words, the correlation between knee pain and OA severity was likely weakened by depressive symptoms [42]. Other studies have emphasized the psychological and social burdens of knee OA, caused by pain and disability [3, 43, 44]. Moreover, poor quality of life (QoL) and perceived need for surgery (PNS) have been associated with depression and social isolation due to OA [3, 4, 43, 45]. On a population
basis, mobility limitations progress slowly, but on an individual basis some people’s function declines quite quickly [46]. Even early in the course of the disease, individuals with knee OA may limit their level of activities [47]. Low to moderate satisfaction with physical leisure activities, travel, hobbies and social events, which are rated as highly important in a person’s life, have been reported because of knee OA and the pain and intrusiveness associated with it [48].

The incidence of depressive symptoms seems to be a common issue in individuals diagnosed with chronic knee OA [3, 41, 49]. Likewise, obesity is a primary modifiable risk factor for knee OA [5, 50, 51] and is closely linked to depressive symptoms [42, 52]. However, a few studies have indicated that both Body Mass Index (BMI) and depressive symptoms are associated with knee pain [44, 45, 53].

The objectives of this study were threefold: 1) To examine whether self-reported pain, measured with the WOMAC pain subscale and VAS, of individuals diagnosed with knee OA would change after performance-based tests were completed. We hypothesized that there would be an increase in both self-reported measures of pain after performance-based tests. 2) To assess whether self-reported pain before and after performance-based tests differs between obese and non-obese individuals and whether their self-reported pain would change from before to after the completion of performance-based tests. We hypothesized that obese individuals with knee OA would score higher on pain measures than non-obese individuals and that the VAS, rather than the WOMAC pain, would capture the change in pain for both obese and non-obese individuals with knee OA from before to after the completion of performance-based tests. 3) To observe whether depressive symptoms and BMI are predictive of self-reported pain before and after performance based tests, and are predictive of QoL and PNS at baseline. We hypothesized that the proportion of variance of self-reported pain, explained by depressive symptoms and BMI would increase after performance-based tests and that depressive symptoms and BMI would predict both QoL and PNS at baseline.
4.3 Methods

Ethical approval was obtained from the Health Science Research Ethics Board (HSREB) of Queen’s University. Patients were recruited from the orthopedic surgical case load of one participating orthopedic surgeon at Kingston General Hospital, Kingston, Ontario, Canada. Patients were identified as potential participants for the study by the surgeon during an initial consultation. Those who showed moderate to severe radiological knee OA using the Kellgren-Lawrence Scale [54] were subsequently contacted by a research associate who described the study procedures and invited them to participate in the study once informed consent was obtained.

The patient group consisted of 31 participants between the ages of 50 and 80 years with knee OA. All participants were able to tolerate moderate activity for 60 to 90 minutes. Additionally, they were free from severe comorbidities that would prevent them from participating in the study, such as unstable angina and/or heart disease, uncontrolled blood pressure (systolic pressure > 140 mmHg, diastolic pressure > 90 mmHg) and non-knee OA related mobility restrictions (neurological and musculoskeletal). All 31 participants were eligible for the study and they were scheduled for an initial assessment conducted in a university laboratory. Participants were recruited between March 2013 and October 2013. (For specific information about recruitment, please refer to Appendix F).

Upon arrival at the laboratory, participants were given a letter of information and consent form. If they agreed to participate, their demographic data including height and weight was obtained. Depression was assessed using the Beck Depression Inventory-II (BDI-II). Pain was assessed before (Time 1) and after (Time 2) performance-based tests (i.e., 6 Minute Walk Test [6MWT], Timed Up and Go [TUG] test, stair climbing test) using the Western Ontario McMaster University Index Osteoarthritis for pain (WOMAC pain) and a VAS. Quality of life (QoL) was measured with the short-form (36) health survey (SF-36), and ratings of perceived need for surgery (PNS) were also obtained.
4.4 Outcome Measures

4.4.1 Self-report measures

The BDI-II is a commonly used measure to assess depressive symptoms, and the latest revised version from the original BDI format [55] is a 21-item test presented in multiple choice format, which measures the presence and degree of depression in adults [55]. The BDI-II is widely used as a screening instrument of depression mood for clinical research [45]. The BDI-II evaluates 21 symptoms of depression, 15 of which cover emotions, four cover behavioural changes, and six cover somatic symptoms. The items cover sadness, pessimism, past failure, self-dislike, self-criticism, suicidal thoughts or wishes, crying, agitation, loss of interest, indecisiveness, worthlessness, loss of energy, changes in sleeping patterns, irritability, changes in appetite, difficulty concentrating, tiredness or fatigue, and loss of interest in sex [56]. Each answer is scored on a scale of 0 – 3. A total score of 0 – 9 indicates no depression, 10 – 18 indicates mild-moderate depression, 19 – 29 indicates moderate-severe depression and 30 – 63 indicates severe depression [56].

Pain was assessed using two measurements: The first was a VAS. The VAS is a measurement tool that indicates the amount of a pain an individual experiences measured across a continuum of values [57]. The scoring range was measured from 0 (no pain) to 10 (highest pain level). The participants were asked to grade the amount of pain they experienced by indicating it on a horizontal line between 0 and 10. The VAS was used to record participants’ perceived level of pain before and after all performed-based tests were completed. The VAS has been validated for pain [58] and has been used in previous studies of joint replacement patients [57, 59]. The second pain measurement was the Likert scale version of the WOMAC subscale for pain [60, 61], which asks about pain experienced over the past 72 hours [4]. This subscale consists of 5 items on a scale of 0 (none) to 4 (extreme) with a total score ranging from 0 to 20. Higher scores indicate greater levels of pain.

The SF-36 is a validated general health related QoL questionnaire [62]. It includes one multi-item scale that measures eight health concepts: general health (GH), vitality (VT), role physical (RP), physical functioning (PF), emotional health problems (RE), social functioning (SF), mental health (MH) and
bodily pain (BP) [62-64]. Patients were asked to report whether their health at the present time limits them in a variety of activities ‘a lot’, ‘a little’ or ‘not at all’. Activities include vigorous and moderate activities, climbing stairs, walking and self-care. The raw score obtained was converted into a new score from 0 to 100, with 0 representing a very low level of QoL on that item and 100 representing a very high QoL on that item [62]. The total score of each health concept was averaged and eight final scores were obtained [65]. The eight health concepts are commonly considered to form two distinct higher-ordered clusters: the physical and mental [65-68]. Factor analytic studies have shown that the physical and mental health factors account for 80-85% of the reliable variance in the eight health concepts [65, 67, 69, 70]. As such, the scores of the health concepts were averaged into two groups called the Physical Component Summary (PCS; made up of the averaged scores of the PF, RP, BP and GH) and the Mental Component Summary (MCS; made of the averaged scores of the VT, SF, RE and MH) [65, 68, 71].

In this study, the PNS was used to measure patients’ level of perceived need for surgery such as total knee replacement surgery. The participants were asked at baseline whether they thought they needed surgery at that point and the answer was obtained on a scale from 0 to 10, 0 being no need for surgery and 10 being the highest need for surgery.

### 4.4.2 Imaging examination

The KL scale method of radiographic examination [54] was used to score the severity of knee OA and to detect differences between groups. KL is the earliest and by far the most commonly used global scale that gives an overall score of OA severity ranging from zero to four [54, 72]. The confirmation of several features were graded as an evidence of OA: grade 0, no radiographic findings of OA; grade 1, possible osteophytes and doubtful narrowing of joint space; grade 2, definite osteophytes and narrowing of joint space; grade 3, moderate multiple osteophytes and definite narrowing of joint space; and grade 4, large osteophytes and marked narrowing of joint space [54]. Both tibiofemoral compartments of the knee were assessed using a standard set of radiographs for reference [54].
4.5 Performance-based tests and physiological test

Three performance-based tests of physical functioning and one physiological test were obtained during a single testing session. The functional tests consisted of the Six Minute Walking Test (6MWT), Timed Up and Go Test (TUG), and the modified Margaria stair climbing test [73]. Peak of oxygen consumption (VO$_2$peak), based on a nomogram previously used [74, 75] for calculation of upper body aerobic power with an arm ergometer, was the physiological test used.

The 6MWT is generally conducted in an enclosed, quiet corridor on a 25-meter track delineated by two lines marked on the floor [76]. Patients were instructed to walk from one line to the other, covering as much ground as possible in six minutes. Individuals were told that they could rest if they became too short of breath or tired, but to continue walking when they were able to do so. To calculate the walking distance, a metre wheel was used to measure the additional steps of any incomplete lap (in meters). The procedure for the TUG requires documenting the time, in seconds, that an individual takes to rise from a standard armchair, walk 3 meters, turn, walk back to the chair and sit down [77]. The participants were allowed to use any assistive devices that they would normally use for walking, to make them feel safe and comfortable during the test. Prior to testing, the subjects were warned that there would be two test trials and then they were instructed about the basic sequence of the test as follows: “When I say, ‘go’, you will stand up pushing from the arm of the chair, walk to the mark (line) on the floor, turn around, walk back to the chair and sit down. I will be timing you using a stopwatch.” The subjects were allowed to rest, as much as they needed, between each trial. The average of these two trials was used as the final score. A shorter time taken to complete the task indicates a lower risk for falling and greater functional status.

Lower limb mechanical power output was assessed by a stair climbing test. This test is a modified version from the original test proposed by Margaria et al. [78] and has been previously validated in obese individuals [79-81]. Participants were asked to climb one step at time, at the highest speed possible. Even though they were allowed to use railings, they were encouraged to use them only if they felt it was extremely necessary. A staircase of 13 steps covering a total vertical distance of 2.0 meters was used. The
final climbing time of the participants was obtained with a stop watch. The average mechanical power (W) can be calculated by multiplying body mass (BM), gravity (g) and vertical distance (h) and dividing its outcome by time (t).

The arm ergometry test was used to predict the VO\(_2\)peak in participants with knee OA. The participants were asked to pedal at a frequency of 70 revolutions per minute (rpm) against a constant workload of 21 Watts (125kg/min) for females and 42 Watts (250kg/min) for males. The workload was adjusted and maintained using the weights from the arm ergometer [75, 82]. To predict VO\(_2\)peak using an arm cycling submaximal test, the subjects should achieve a continuous steady state heart rate either equal to or above 110 beats per minute (bpm) during the last 30 seconds of submaximal test [75]. Heart rate was monitored constantly using a chest strap heart rate monitor and a digital watch set (Polar Electro, Inc Woodbury, NY) during the test. The test’s length of time was four minutes and pulse rate was recorded every 10 seconds during the last 30 seconds, between the third and fourth minutes. If the difference between the lowest and the highest pulse rate, recorded in the last 30 seconds of exercising, did not exceed 5bpm, a steady state heart rate was considered to be present [74, 75]. The average HR, from the steady state, was used to find a corresponding VO\(_2\)peak (L.min) on the nomogram. Further to that, VO\(_2\)peak was calculated in ml/kg/min based on the nomogram’s equation: \(\text{VO}_2\text{peak (L.min)} \times 1000 / \text{Body Weight (BW)}\). All of the participants reached at least 110bpm or more; consequently, a new test was not needed. However, if their heart rates had not reached at least 110bpm during the last 30 seconds of testing, the workload would have been increased by 21 W (125 kg/min) and a new test would have been initiated.

4.6 Data Analysis

Data were analyzed using the Statistical Package for the Social Sciences version 21 (SPSS 21) and Microsoft Excel 2010. The alpha (\(\alpha\)) level was set at \(p < 0.05\). Results are presented as mean ± standard deviation (SD) unless otherwise specified.
4.6.1 Manipulation checks and group composition analyses

Of the 31 participants diagnosed with knee OA, 15 were considered obese (BMI $\geq 30$ kg/m$^2$) and 16 were non-obese. Specifically, of the 16 non-obese participants, 9 were overweight (BMI$= 25$–$29.9$ kg/m$^2$) and 7 were healthy weight (BMI$= 18.5$–$24.9$ kg/m$^2$). A one-way ANOVA between overweight and healthy weight participants with knee OA demonstrated that they did not differ significantly on any demographic or main variables of interest, including radiographic examination findings (p’s $>.05$). Likewise, a chi-square analysis did not reveal any significant difference in gender (p $>.05$) between the overweight and healthy weight groups. Therefore, we combined the overweight and healthy weight groups into one group: the non-obese OA group. Radiographic examination was obtained from all 31 participants diagnosed with knee OA. A one-way ANOVA between the obese OA and non-obese OA groups was conducted to examine whether knee OA severity was significantly different between these two groups. The analysis indicated no significant differences between-groups on knee OA severity at baseline (p $>.05$). See Table 4.1.
<table>
<thead>
<tr>
<th>Baseline information / Group</th>
<th>Obese OA</th>
<th>Mean (SD)</th>
<th>Minimum</th>
<th>Maximum</th>
<th>F</th>
<th>P-value</th>
</tr>
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<tr>
<td>Age</td>
<td>Obese OA</td>
<td>65.9 (8.3)</td>
<td>50</td>
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<td>Non-obese OA</td>
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<td>62</td>
<td>81</td>
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<td></td>
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<tr>
<td>BMI</td>
<td>Obese OA</td>
<td>39.0 (8.4)</td>
<td>29.3</td>
<td>62.1</td>
<td>24.4</td>
<td>0.000</td>
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<td></td>
<td>Non-obese OA</td>
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<td>23.4</td>
<td>28.4</td>
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<tr>
<td>Body Weight</td>
<td>Obese OA</td>
<td>104.3 (19)</td>
<td>70</td>
<td>143.7</td>
<td>28.8</td>
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<tr>
<td></td>
<td>Non-obese OA</td>
<td>76.8 (11.2)</td>
<td>62</td>
<td>82</td>
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<tr>
<td>X-Ray (KL)</td>
<td>Obese OA</td>
<td>3.3 (0.97)</td>
<td>2.0</td>
<td>4.0</td>
<td>.056</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>Non-obese OA</td>
<td>3.3 (0.8)</td>
<td>2.0</td>
<td>4.0</td>
<td></td>
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<tr>
<td>BDI-II</td>
<td>Obese OA</td>
<td>18 (5.5)</td>
<td>11</td>
<td>27</td>
<td>38.6</td>
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<td>Non-obese OA</td>
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<td>PNS</td>
<td>Obese OA</td>
<td>7.7 (2.0)</td>
<td>4</td>
<td>10</td>
<td>25.1</td>
<td>0.000</td>
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<tr>
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<td>Non-obese OA</td>
<td>4.0 (2.1)</td>
<td>0</td>
<td>8.2</td>
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<td>PCS</td>
<td>Obese OA</td>
<td>30.5 (15.2)</td>
<td>12.3</td>
<td>64.2</td>
<td>11.6</td>
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<td>Non-obese OA</td>
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<td>30.4</td>
<td>87.1</td>
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<td>MCS</td>
<td>Obese OA</td>
<td>57.1 (20.8)</td>
<td>19.6</td>
<td>79.5</td>
<td>5.1</td>
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<td>42.3</td>
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<td>Stair Climbing</td>
<td>Obese OA</td>
<td>171.5 (66.1)</td>
<td>79.95</td>
<td>344.00</td>
<td>30.5</td>
<td>0.000</td>
</tr>
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<td>Non-obese OA</td>
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<td>28.47</td>
<td>18.4</td>
<td>0.000</td>
</tr>
<tr>
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<td>Non-obese OA</td>
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<td>14.28</td>
<td>36.56</td>
<td></td>
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<tr>
<td>TUG</td>
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<td>11.0 (2.8)</td>
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<td>18.94</td>
<td>21.3</td>
<td>0.000</td>
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<td>5.17</td>
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<td>425.0</td>
<td>30.5</td>
<td>0.000</td>
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<td>Non-obese OA</td>
<td>447.7 (65.6)</td>
<td>325.0</td>
<td>555.0</td>
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</tbody>
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Table 4.1: (SD) Standard deviation; x–Ray (Kellgren – Lawrence or KL); Age (yrs.); BMI (kg/m²); Body Weight (Kg); BDI-II: Beck Depression Inventory – Higher score = more depression; Physical and Mental Component Summary (PCS and MCS) – Quality of Life – higher score better QoL; PNS (Likert scale from 0 – no intent to undergo surgery to 10 high intent to undergo surgery; Stair Climbing - Lower limb mechanical power- Watts (W); Six Minute Walking Test (6MWT) – meters (m); Timed Up and Go Test (TUG) – seconds (s); Peak of oxygen consumption (VO2peak) – (ml.kg/min). Obese OA (N = 15) and Non-obese OA (N= 16) All significant values between groups were (p < 0.05)
Further analyses between obese OA and non-obese OA groups indicated that body weight (F (1, 29) = 24.4; p ≤ .0001) and BMI (F (1, 29) = 28.8; p ≤ .0001) were significantly different between groups (Table 4.1). Analyses indicated that BDI-II (F (1, 29) = 38.6; p ≤ .0001), PNS (F (1, 29) = 25.1; p ≤ .0001), PCS – QoL (F (1, 29) = 11.6; p ≤ .002) and MCS – QoL (F (1, 29) = 5.1; p ≤ .032) were significantly different between groups at baseline (Table 4.1). The three performance-based tests (stair climbing, 6MWT, and TUG) and the VO\textsubscript{2}peak (physiological test) were also compared between obese OA and non-obese OA groups. Analyses indicated that results from the stairs climbing test (F (1, 29) = 21.3; p ≤ .0001), 6MWT (F (1, 29) = 30.5; p ≤ .0001), TUG (F (1, 29) = 18.4; p ≤ 0.0001) and the VO\textsubscript{2}peak (F (1, 29) = 30.5; p ≤ .0001) were significantly different between groups (Table 4.1).

4.7 Results

In order to test our first hypothesis that self-reported pain would be higher after performance-based tests, two repeated measures ANOVAs were conducted. The repeated measures ANOVA examined whether the WOMAC pain subscale score and the VAS ratings of all 31 participants changed from before (Time 1) to after (Time 2) performance-based tests (Figure 4.1). Results indicated that the WOMAC pain subscale score changed significantly (F (1, 30) = 7.1; p = .012) by increasing from Time 1 (mean = 8.3, SD = 3.2) to Time 2 (mean = 9.7, SD = 4.6). The VAS ratings also increased significantly (F (1, 30) = 85; p ≤ .0001) from Time 1 (mean = 2.9, SD = 1.5) to Time 2 (mean = 4.0, SD = 1.4) (Figure 4.1).
In order to test our second hypothesis that obese individuals with knee OA would score higher on pain measures than non-obese individuals, and that the VAS pain, rather than the WOMAC pain, would capture change in pain from Time 1 to Time 2 for both groups of individuals with knee OA, we conducted a repeated measures ANOVA that examined whether the obese OA group had higher scores on the WOMAC pain subscale (Figure 4.2) and the VAS (Figure 4.3) as compared to the non-obese OA group. The results indicated that the WOMAC pain score (F (1, 29) = 24; p < .0001) and VAS pain (F (1, 29) = 29; p < .0001) were significantly different between groups, with the obese OA group demonstrating higher WOMAC pain subscale scores (mean = 11.5) and VAS ratings (mean = 4.5) as compared with the non-obese OA group (mean WOMAC pain subscale score = 6.6 and mean VAS rating = 2.5). The within-groups factor examined whether the mean scores of each group changed after performance-based tests were completed and it indicated that only the obese OA group significantly increased from Time 1 to Time 2 when pain was measured with the WOMAC pain subscale (means = 9.8 and 13.3; F (1, 29) = 12; p = .002). No change was observed on the WOMAC pain subscale score for the non-obese OA group (Figure 4.2). However, the within-group factor for the VAS ratings indicated that the obese OA group

Figure 4.1: Self-reported pain of 31 individuals diagnosed with knee: WOMAC pain significantly changed from time 1 to time 2 (*), p = .012 VAS rating significantly changed from time 1 to time 2 (**), p ≤ 0.0001
(means = 3.9 and 5.1; F (1, 14) = 76; p < .0001) and the non-obese OA group (means = 1.9 and 3.1; F (1, 15) = 28; p < .0001) significantly increased after performance-based tests were completed (Figure 4.3).

Figure 4.2: WOMAC pain: 15 obese OA and 16 non-obese OA: Between groups: the obese OA group demonstrated significantly higher WOMAC pain than the non-obese OA group p ≤ 0.0001. Within groups: WOMAC pain significantly change from time 1 to time 2, but only in the obese OA group; (*), p = .002
In order to test our third hypothesis that the proportion of variance of self-reported pain, explained by depressive symptoms and BMI would increase after performance-based tests, we conducted four stepwise regression analyses before (Time 1) and after (Time 2) the completion of performance-based tests. Prior to the analyses, we ensured that there was no evidence of strong multicollinearity among the independent variables (all Pearson correlation coefficients (r) were < 0.80) [83]. At Time 1, the stepwise regression analysis indicated that depressive symptoms alone explained a significant proportion of variance of the WOMAC pain, $R^2 = 27\%$, $F(1, 29) = 10.8$; $p = .003$. Likewise, at Time 2 depressive symptoms alone also explained a significant proportion of variance of the WOMAC pain, $R^2 = 35.7\%$, $F(1, 29) = 16$; $p < .0001$; however, a higher proportion of variance explained was observed at Time 2 compared to Time 1 (Table 4.2). For the VAS ratings, the stepwise regression analysis at Time 1 indicated that depressive symptoms and BMI explained a significant proportion of variance of the VAS ratings, $R^2 = 46.7\%$, $F(1, 29) = 12.3$; $p < .0001$, and that at Time 2, both depressive symptoms and BMI also explained a significant proportion of variance of the VAS ratings, $R^2 = 52.6\%$, $F(1, 29) = 15.5$; $p < .0001$. 

Figure 4.3: VAS: 15 obese OA and 16 non-obese OA: Between groups: the obese OA group demonstrated significantly higher VAS than the non-obese OA group $p \leq 0.0001$. Within group: VAS significantly change from time 1 to time 2 for both groups; obese OA (*), $p \leq 0.0001$ and non-obese OA (**), $p \leq 0.0001$. 

![Figure 4.3: VAS](image)
.0001, with a higher proportion of variance explained observed at Time 2 compared to Time 1 (Table 4.2). Findings from the WOMAC pain subscale suggested that depressive symptoms alone explained a significant proportion of variance of the WOMAC pain subscale scores, and that after performance-based tests the proportion of variance increased from 27% to 35.7%. Consequently depressive symptoms alone accounted for 35.7% of variance of the WOMAC pain subscale score after completion of performance-based tests. On the other hand, the results from the VAS ratings indicated that both depressive symptoms and BMI explained a significant proportion of variance of the VAS ratings, and that after performance-based tests the proportion of variance increased from 46.7% to 52.6%. Therefore, depressive symptoms and BMI accounted for 52.6% of variance of VAS ratings after completion of performance-based tests.

<table>
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<tr>
<th>Perceived Need for Surgery</th>
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<tr>
<td><strong>PNS:</strong> Depressive symptoms and BMI explained a significant proportion of variance of the PNS, $R^2 = 55%$, $F (1, 29) = 17.4; p &lt; .0001$</td>
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<tr>
<th>Quality of Life: PCS and MCS</th>
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<tr>
<td><strong>PCS:</strong> Depressive symptoms and BMI explained a significant proportion of variance of the PCS - QoL, $R^2 = 49%$, $F (1, 29) = 13.4; p &lt; .0001$</td>
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<tr>
<td><strong>MCS:</strong> BMI alone explained a significant proportion of variance of the MCS, $R^2 = 23%$, $F (1, 29) = 8.5; p = .007$</td>
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<th>WOMAC pain subscale</th>
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<td><strong>Time 1:</strong> Depressive symptoms alone explained a significant proportion of variance of the WOMAC pain, $R^2 = 27%$, $F (1, 29) = 10.8; p = .003$</td>
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<tr>
<td><strong>Time 2:</strong> Depressive symptoms alone explained a significant proportion of variance of the WOMAC pain, $R^2 = 35.7%$, $F (1, 29) = 16; p &lt; .0001$</td>
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<th>VAS rating</th>
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<tr>
<td><strong>Time 1:</strong> Depressive symptoms and BMI explained a significant proportion of variance of the VAS pain, $R^2 = 46.7%$, $F (1, 29) = 12.3; p &lt; .0001$</td>
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<tr>
<td><strong>Time 2:</strong> Depressive symptoms and BMI explained a significant proportion of variance of the VAS pain, $R^2 = 52.6%$, $F (1, 29) = 15.5; p &lt; .0001$</td>
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Table 4.2: Summary table of Stepwise regression analysis—Depressive symptoms and BMI were predictors of self-reported pain, Perceived Need for Surgery and Quality of life
As part of our third hypothesis that depressive symptoms and BMI would predict both QoL and PNS at baseline, we also conducted a stepwise regression analyses. The three stepwise regression analyses explored whether the variability of QoL (PCS and MCS) and PNS were explained by depressive symptoms and BMI. Results indicated that BDI-II scores and BMI explained a significant proportion of variance of the PCS, $R^2 = 49\%$, $F(1, 29) = 13.4$; $p < .000$, but that BMI alone explained a significant proportion of variance of the MCS, $R^2 = 23\%$, $F(1, 29) = 8.5$; $p = .007$ (Table 4.2). These findings suggest that depressive symptoms and BMI accounted for 49% of variance on the physical component of QoL in patients with knee OA. However, only BMI accounted for 23% variance on the mental component of QoL. In terms of PNS, both the BDI-II scores and BMI explained a significant proportion of variance of PNS, $R^2 = 55\%$, $F(1, 29) = 17.4$; $p < .000$, indicating that depressive symptoms and BMI accounted for 55% of variance of patient’s perceived need for surgery (Table 4.2).

4.8 Discussion

Results demonstrated that both self-report pain scores, measured with the WOMAC pain subscale and VAS ratings were significantly higher after as compared to before the completion of performance-based tests. This pattern of results suggests that both self-report pain measurements, when possible, should be administered to individuals with OA after performance-based tests (Figure 4.1) because it captures participants’ experience of pain in real time. When the sample was divided into obese and non-obese individuals with OA, we observed that the obese group demonstrated significantly higher levels of self-reported pain. The VAS ratings captured a significant increase in pain in both groups from Time 1 to Time 2. The WOMAC pain subscale, on the other hand, only captured change in the obese OA group after completion of performance-based tests. Further analyses indicated that depressive symptoms and BMI explained a significant proportion of variance in VAS ratings, but that depressive symptoms alone explained a significant proportion of variance in the WOMAC pain subscale scores. Moreover, the proportion of variance explained by both self-report pain measurements was higher after completion of
performance-based tests. Finally, depressive symptoms and BMI explained a significant proportion of variance in QoL scores and PNS ratings at baseline.

4.8.1 Increase in self-reported pain after performance-based tests in individuals with knee OA

Previous studies have indicated that performance-based tests are highly associated with knee pain and therefore performance-based tests may influence self-reported pain ratings [29, 61]. In a study comparing pain due to knee OA in women and men [84], the authors found no significant (p = 0.08) difference between women and men at rest, but during a functional testing, such as gait speed test, women had a significantly higher (p = 0.04) level of pain (7.34 ± 5.69) compared to men (5.69 ± 4.95). Self-reported pain ratings can be obtained at rest, during functional tests or immediately after a test [19, 22, 29, 85, 86]. However, studies have [84] indicated that, when obtained during functional tests, knee pain ratings had a larger impact in sex differences. In addition, we suggest that in general, individuals diagnosed with chronic knee OA will likely not report pain levels as accurately when recalling the pain, as compared to when reporting on pain levels in real-time; that is, when they find themselves exposed to a situation in which pain is triggered, as observed in our results.

Even though the WOMAC pain score and the VAS ratings are reliable tools to measure pain in individuals with knee OA [30], the way in which the pain experience is captured by each measurement may influence its final outcome [28]. The WOMAC is generally obtained before or a few minutes after the completion of performance-based tests [87]. While the VAS rating can be obtained before performance-based tests, it is typically obtained during or right after performance-based tests in clinical assessments [29, 30]. Taking into consideration that knee pain during a performance-based test could be a “momentary physical experience,” it seems logical to capture the experience of pain when it occurs, as measured with the VAS rating, rather than few minutes later (as measured with the WOMAC pain subscale), when some of that physical experience had receded. However, our results indicated that scores on both self-reported pain measures significantly increased after performance-based tests. These findings
suggest that capturing knee pain immediately after performance-based tests with the VAS rating, or a few minutes later with the WOMAC pain subscale did not affect the final outcome (Figure 4.1). Nevertheless, we suggest that both self-report pain measures, when possible, should be administered to individuals with OA after performance-based tests as they capture participants’ experience of pain in real time.

4.8.2 Change in self-reported pain in obese and non-obese individuals after performance-based tests

When examining our full sample of 31 individuals with knee OA, we observed that after performance-based tests both the WOMAC pain subscale score and the VAS rating significantly increased. However, when we compared our sample between obese and non-obese individuals with knee OA, differences emerged. First, results indicated that obese individuals with knee OA scored higher on both the WOMAC pain subscale and VAS measures than non-obese individuals. Second, findings suggested that after performance-based tests, only the obese OA group had a significant increase in knee pain when pain was assessed with the WOMAC pain subscale (Figure 4.2). On the other hand, both groups had a significant increase in knee pain when pain was measured with the VAS (Figure 4.3).

Previous studies have indicated that obesity is a risk factor for progression of knee OA by decreasing function and increasing pain [5, 50, 88]. A meta-analysis of previous weight loss studies suggested that at least 10% of body weight loss is needed to have a considerable clinical effect on pain and physical function [89]. According to Felson et al. [37], if obese men lost enough weight to fit into the overweight category and that if overweight men lost enough weight to be within the reference BMI range of < 25kg / m², symptoms in knee OA would drop about 21.4%. In women with the same condition, they drop would be even more, by about 33%. Moreover, being obese increases the load placed on the knee joints, which increases joint stress and pain during walking activities [40]. This pattern of findings support our results that obese individuals tend to experience higher levels of pain compared to non-obese individuals with knee OA. However, there are no previous studies indicating whether one pain measure should be preferable over another when assessing knee pain in obese individuals with knee OA.
When pain was assessed in all participants, we observed no differences when capturing knee pain right after performance-based tests with the VAS rating or a few minutes later with the WOMAC pain subscale. However, when the sample was divided into obese and non-obese groups, the WOMAC pain subscale was limited in detecting changes in pain only in the obese OA group. There is consistent evidence demonstrating that the WOMAC subscales of pain and physical function are more influenced by the ability to perform activity than by the patients’ experience of pain and their perception of difficulty to perform daily activities [90, 91]. Therefore, because the non-obese individuals with OA were capable of performing functional activities significantly better with significantly less pain than those in the obese OA group (as we observed in our study, see Table 4.1), we did not expect significant changes on the WOMAC pain subscale for the non-obese OA group. Moreover, a previous study indicated that the WOMAC pain subscale may capture more than just knee pain, suggesting that the WOMAC pain could be influenced by the presence of fatigue, depression and back pain [92]. The authors indicated that WOMAC scores, including the pain subscale score, should be interpreted with caution. Furthermore, psychological factors should be considered when rheumatic diseases are assessed [92]. Based on our findings, the VAS pain rating seems to be more accurate than the WOMAC pain subscale score when pain is assessed during or right after functional activities [87]. Therefore, we suggest that the VAS pain rating may be a better tool for assessing knee pain of individuals diagnosed with knee OA during or right after performance-based tests, because it captures the pain at the moment of its occurrence.

4.8.3 Depressive symptoms, quality of life and need for surgery in individuals with knee OA

Excessive body weight and depressive symptoms are commonly observed in individuals diagnosed with knee OA compared to the general population [41, 49], and are both positively associated with pain and activity limitations [93, 94]. Our results indicated that depressive symptoms alone explained a significant proportion of variance of self-reported pain before ($R^2 = 27\%$, $p = .003$) and after ($R^2 = 35\%$, $p < .0001$) performance-based tests, as measured by the WOMAC pain subscale (Table 4.2).
However, when we assessed knee pain using the VAS, both depressive symptoms and BMI explained a significant proportion of the variance in self-reported pain, and the results obtained before ($R^2 = 46.7\%, \ p < .0001$) and after ($R^2 = 52.6\%, \ p < .0001$) performance-based tests were higher than the ones obtained when knee pain was assessed with the WOMAC pain subscale (Table 4.2). Even though the VAS rating revealed a higher proportion of variance explained by depressive symptoms and BMI compared to the WOMAC pain subscale score (Table 4.2), these results do not necessarily mean that the findings from the WOMAC pain subscale are not important. The WOMAC pain subscale is widely used in research and clinical settings [4, 41, 43] and based on our results, its use was not limited to detecting change in pain in obese individuals.

A recent study found that pain due to OA strongly predicted future fatigue and disability (both short and long term), and that fatigue and disability in turn predicted future depressive symptoms [3]. Therefore, persons living longer with the burden of knee OA, particularly those who are obese, may report depressive symptoms and thus the potential occurrence of a pain-depression cycle should be recognized from a clinical point of view. Moreover, previous studies in individuals with knee OA observed the effect of weight loss on depression, quality of life and functional activity [3, 4, 7, 28, 89]. These studies indicated that after a significant body weight loss, quality of life, depression and functional capacity may improve. One particular study examined the relationship between depression and functional status of overweight and obese patients with knee OA. They found that levels of depression were significantly associated with WOMAC subscale scores: function ($r = 0.54; \ p < 0.001$), stiffness ($r = 0.26; \ p = 0.004$) and pain ($r = 0.43; \ p < 0.001$) [28]. They also indicated that obese individuals with moderate to high depressive symptoms had a higher WOMAC pain score and demonstrated poorer performance in functional tests compared to obese individuals without depressive symptoms [28]. Similar to our findings, our obese OA group, who reported depressive symptoms, also had high WOMAC pain scores before and after performance-based tests (Figure 4.2). Moreover, our obese OA groups also performed significantly ($p \leq 0.0001$) worse in functional test compared to our non-obese OA group. Together these studies established an important link between depression and obesity to explain pain and disability, suggesting
that treatment of depression and successful weight loss management may improve knee pain and function [4, 7, 89, 95].

A recent study found that preoperatively, the prevalence of anxiety and depressive symptoms was high in individuals diagnosed with knee and hip OA [96]. It was also observed that after 3 to 12 months postoperatively, the prevalence of anxiety and depressive symptoms decreased from 27.9% to 10.8% in patients diagnosed with hip OA and from 22.7% to 11.7% in patients with knee OA [96]. However, patients who indicated higher levels of depressive symptoms preoperatively also had worse outcomes 3 to 12 months after surgery. In agreement with the aforementioned study [96], we observed that depressive symptoms and BMI explained a significant proportion of variance of PNS and QoL and those with higher level of depressive symptoms also had lower functional performance. A previous study with 34 obese women diagnosed with knee OA investigated whether weight loss was associated with a reduction in PNS for total knee replacement (TKR) surgery [4]. The authors found that, after significant reduction of body weight followed by decrease in knee pain, a significant decrease in PNS was observed at 6 weeks, where 60% of the participants considered surgery. At 6 months, only 29.4% of the participants were still considering surgery [4]. The same study also indicated that the health concepts from the QoL questionnaire, such as physical function (PF) and body pain (BP), significantly (r=0.66; p < 0.0001 and r=0.52; p < 0.0001) correlated with body weight over time. As weight loss was achieved, over time, the health concepts of PF (p < 0.0001) and BP (p < 0.0001) significantly improved [4].

A cross-sectional study in patients with clinical knee OA indicated that both BMI and depressive symptoms seemed to be independently associated with knee pain and activity limitations [44]. Even though the results suggested that the contribution of BMI to activity limitations were more substantial (20.4%) than that of depressive symptoms (2.6%), the authors found that both BMI and depressive symptoms explained knee pain poorly [44]. It is well-known that excessive weight is a contributing factor causing activity limitations and disability [62, 63], and activity limitations are usually a consequence of knee pain in individuals diagnosed with knee OA [2, 3, 5, 12]. Likewise, knee pain and depressive symptoms are key factors that increase disability in older individuals with knee OA [3, 42]. Therefore, it
seems contradictory that both BMI and depressive symptoms explained knee pain poorly. Although we did not use BMI and depressive symptoms to predict activity limitations, in agreement with previous research studies [15, 28, 96-98], our findings revealed that both BMI and depressive symptoms were strongly associated with knee pain before and after performance-based tests (Figure 4.1). For that reason, our results suggest that depressive symptoms and BMI are important predictors of knee pain, particularly when assessed with a VAS right after performance-based tests. We also suggest that poor QoL and increased PNS are likely explained by depressive symptoms and BMI, and obese individuals with knee OA may experience higher levels of pain, perceive lower QoL and indicate a higher need for surgery, compared to their non-obese counterparts.

4.9 Limitations, future directions, and conclusions

During some stages of our study we encountered some limitations such as lack of funds to intensify recruiting and consequently increase sample size. We also had difficulty recruiting patients within a BMI category of 18.5-24.9 kg/m². Finally, some patients refused to participate because they live in rural areas and rely on family for transportation. However we obtained important findings of significant impact and relevance to the clinical setting. Future studies should include a larger sample size with a longitudinal design. This type of study would provide additional information about long-term changes in pain, QoL and PNS in individuals with knee OA. Further investigations should focus on treatment for depression and weight loss therapy and try determining whether a combination of treatments is more effective than treating obesity or depressive symptoms individually. Future research should also measure the impact of reduction in depressive symptoms and body weight on physical health and well-being of individuals with knee OA before and after total knee replacement surgery.

In conclusion, we observed that individuals diagnosed with knee OA show higher levels of knee pain measured with the WOMAC pain subscale and VAS rating after performance-based tests. Therefore, assessment of pain, when possible, should be administered to individuals with OA after performance-based tests. Moreover, when the sample was divided into obese and non-obese individuals with OA, the
WOMAC pain subscale did not capture change in pain in non-obese individuals. Therefore, the VAS pain rating may be a better tool for assessing knee pain of obese and non-obese individuals diagnosed with knee OA during or right after performance-based tests, because it captures the pain at the moment of its occurrence. In addition, clinicians should encourage obese patients with knee OA to lose weight and those who are not obese to maintain a healthy weight. Finally, depressive symptoms are also predictive of increased pain before and after functional tests, with higher levels of depression predicting worse reports of pain. Clinicians should be aware of signs of depression as a potential predictor of decreased quality of life and increased perceived need for surgery in individuals with knee OA, especially those who may be obese. Therefore, treatment of depression and a successful weight loss management may be necessary to improve the lifestyle of some individuals with knee OA.
4.10 References


Chapter 5
Measurement of isokinetic quadriceps muscle strength and pain in knee osteoarthritis


5.1 Abstract

**Background:** Quadriceps muscle weakness and knee pain are considered important factors in physical disability of individuals with knee osteoarthritis (OA). As the population with knee OA becomes more obese and sedentary, muscle weakness and knee pain may contribute to a greater decrease in functional performance.

**Objectives:** The purposes of this study were three-fold. First, to investigate whether muscle weakness assessed under different isokinetic angular velocities differs among individuals who are obese and non-obese and who have been diagnosed with knee osteoarthritis (OA). Second, to examine whether knee pain changed in individuals with knee OA from before to after the test was completed. Third, to examine whether quadriceps strength and BMI would predict performance-based tests of individuals with knee OA.

**Methods:** The study included thirty one participants diagnosed with radiographic knee OA by an orthopedic surgeon using the Kellgren-Lawrence Scale and 15 control health individuals. In order to measure muscle strength our sample was divided in three groups: obese OA, non-obese OA and healthy control individuals, the control individuals were used as a comparison group for muscle strength. Knee pain, was measured with VAS before and after isokinetic muscle testing at the angular velocities of 60°/s, 90°/s and 120°/s between obese OA and non-obese OA groups only.

**Results:** There was a statistically significant difference in isokinetic peak torque between the OA and control groups at each angular velocity (p < 0.001) at 60°/s, ( p < 0.001) at 90°/s and (p < 0.001) at 120°/s. However, further analysis indicated that only at 60°/s of the isokinetic peak torque of between
obese OA and non-obese OA were statistically significant different from each other. Knee pain significantly increased $p < 0.0001$ from before to after isokinetic muscle strength testing, but only at the angular velocity of $60^\circ/s$. No significant differences in pain were observed under the angular velocities of $90^\circ/s$ and $120^\circ/s$. BMI, not the isokinetic peak torque, explained the proportion of variance of the 6MWT, the TUG, and VO$_2$peak. The stair climbing test was the only test that had the proportion of variance explained by isokinetic peak torque.

**Conclusion:** The angular velocity of $60^\circ/s$ may be an optimal velocity at which to differentiate muscle weakness and knee pain between obese and non-obese individuals with OA. Obesity, not quadriceps muscle weakness, seems to be a better predictor of impaired function. Therefore, performance ability might be more impaired as a direct consequence of obesity rather than muscle weakness.

### 5.2 Introduction

Quadriceps strength declines with age, and aging is a risk factor for the development and progression of knee osteoarthritis (OA) [1-3]. Quadriceps muscle weakness is also considered an important factor in physical disability and pain in individuals with knee OA [2]. Consequently, for those over the age of 65, knee OA accounts for greater levels of joint pain and physical disability in lower extremity tasks, such as walking, stair climbing, and rising from a chair, than any other condition [4, 5]. Another well-known risk factor for knee OA development is obesity [6, 7]. However, despite evidence that obesity may affect soft tissues, such as muscles and tendons [8-10], the majority of studies have focused on the impact of obesity on bone and joint disorders such as fractures and joint malalignment [11, 12]. Therefore, it is important to assess whether knee extensor muscle weakness, and the experience of pain associated with it, affect both obese and non-obese individuals with knee OA.

Isokinetic dynamometers are commonly used to assess knee muscle strength [7, 13-15]. The term “isokinetic” is defined as a dynamic muscular contraction set at a constant velocity during movement and generally controlled by a special device [16]. The advantages of isokinetic systems include constant pre-
selected velocity of movement and resistance on the device equal to muscular force [16, 17]. These unique features provide safety when used for research purposes and for the rehabilitation of patients with muscular and ligamentous injuries. These features also allow for accuracy in the assessment of muscular performance at different functional velocities of movement [16].

Isokinetic muscle strength testing has included angular velocities ranging from 30°/s to 180°/s in studies of persons with knee OA [1, 13, 17, 18]. However, the most common isokinetic testing velocities reported in these studies were 60°/s, 90°/s and 120°/s [1, 13, 17, 18]. Reliability tests have been reported in the literature for these three angular velocities in healthy individuals and those with knee OA [19, 20]. However, the muscular torque exerted during isokinetic testing decreases with increasing angular velocity of movement [16], suggesting that individuals with knee OA, who commonly show decreased quadriceps strength [1, 14], may demonstrate decreased muscle strength when assessed at lower velocities, such as 60°/s. Therefore, when quadriceps muscle strength is assessed at the angular velocity of 60°/s differences between obese and non-obese individuals with knee OA may become more evident.

Two studies examined whether muscle strength and body weight were associated using angular velocities of 60°/s and 120°/s in obese and non-obese individuals with knee OA [21, 22]. Slemenda et al. [21] indicated that knee OA was associated with an increase in body weight in women (P = 0.0014) but not in men. They further reported that among the 13 women who developed incident OA, there was a strong, highly significant negative correlation between body weight and knee extensor muscle strength (r = -0.74, P = 0.003). On the other hand, Segal et al. [22] indicated that peak quadriceps strength did not significantly differ by BMI or by the presence of knee OA. The authors suggested that factors other than strength might mediate the association between obesity and knee OA. These conflicting findings suggest that the relationship between obesity and lower extremity muscle strength needs to be further explored. As such, it would be important to identify whether isokinetic muscular testing differs between obese and non-obese individuals with knee OA, at different angular velocities.

Symptomatic knee OA is characterized by consistent presence of joint pain [23, 24]. However, the experience of pain observed during muscle strength testing has not been studied extensively in those
with knee OA [17]. It is not known whether quadriceps muscle weakness precedes or follows joint pain, or whether pain is mediated by disuse atrophy or by physiological mechanisms that inhibit muscle contraction [25, 26]. However, an increase in knee pain is typically observed after functional activities, particularly activities requiring quadriceps activation, such as going up stairs or standing from a chair [4, 5, 27]. These findings suggest that quadriceps weakness is associated with knee pain. In one study examining this issue, Lankhorst et al. [28] expected that individuals with lower levels of knee pain would produce greater peak torques. The authors assessed knee pain after isometric knee extension, tested at 90° of knee flexion, and after isokinetic knee flexion and extension at angular velocities of 30°/s, 60°/s, 120°/s and 180°/s. Unexpectedly, their results indicated very small negative correlations between torque production at any velocity and pain experienced during the specific strength tests. The authors concluded that the influence of momentary pain on torque production was minimal [28]. Another study examined whether knee pain was dependent on angular velocity during isokinetic testing on individuals with knee OA [17]; although they observed that at the angular velocity of 60°/s the peak torques were significantly higher than at 90°/s and 120°/s, the authors found a large variation of pain across different angular velocities. They were therefore unable to conclude that knee pain was significantly different at different angular velocities [17]. Despite important findings from both studies [17, 28], the issue of obesity was not considered in these studies.

Obese individuals diagnosed with knee OA tend to score poorly on performance-based tests [29-32]. For example, walking is often impaired as a direct consequence of obesity through excess weight-bearing [33]. In addition, obesity is also a major risk factor for knee OA development [34, 35]. Therefore, the ability to walk may be worse in obese individuals with knee OA, but not necessarily better in obese individuals without knee pain. Consequently, it is important to observe whether obesity and lower quadriceps muscle strength can predict performance-based tests such as walking, stair climbing, and the Timed Up and Go test (TUG), that simulate tasks of daily activities.

Therefore, the objectives of this study were three-fold: 1) To examine whether the average peak torque of isokinetic muscular testing of the quadriceps differs between obese and non-obese individuals
with knee OA and healthy control individuals, at three different angular velocities: 60°/s, 90°/s and 120°/s. We hypothesized that only at the angular velocity of 60°/s obese and non-obese individuals with knee OA and healthy control participants would significantly differ from each other. The muscular torque exerted during isokinetic testing is normally higher at lower angular velocity of movement [16], suggesting that at a lower angular velocity decreased muscle strength of obese and non-obese individuals with knee OA may be more evident. 2) To examine whether knee pain, measured with the visual analogue scale (VAS), would change after isokinetic muscle strength testing, at the angular velocities of 60°/s, 90°/s and 120°/s, and whether such change would be experienced by obese and non-obese individuals with knee OA. We hypothesized that only at the angular velocity of 60°/s that both obese and non-obese individuals with knee OA would experience an increase in pain. For the same reason as in our first objective, at a lower angular velocity, when individuals exert higher muscular torque, an increased level of pain is expected. 3) To examine whether quadriceps muscle strength, as measured by the peak torque of isokinetic muscle testing, and BMI would predict performance-based tests of individuals with knee OA. Since no other previous research has used isokinetic muscle strength and BMI as a predictor for performance-based tests in obese and non-obese individuals with knee OA, no hypothesis was stated; this issue was explored as a research question of interest.

5.3 Methods

Ethical approval was obtained from the Health Science Research Ethics Board (HSREB) of Queen’s University. Patients were recruited from the orthopedic surgical case load of one participating orthopedic surgeon at Kingston General Hospital, Kingston, Ontario, Canada. Patients were identified as potential participants for the study by the surgeon during an initial consultation. Those who showed moderate to severe radiological knee OA using the Kellgren-Lawrence Scale [36] were subsequently contacted by a research associate who described the study procedures and invited them to participate in the study once informed consent was obtained.
The patient group consisted of 31 participants between the ages of 50 and 80 years with knee OA. The control group consisted of 15 participants within a similar age range and who had no complaints of knee pain. The control group was recruited from the local community through advertisements. All participants were able to tolerate moderate activity for 60 to 90 minutes. Additionally, they were free from severe comorbidities that would prevent them from participating in the study, such as unstable angina and/or heart disease, uncontrolled blood pressure (systolic pressure > 140 mmHg, diastolic pressure > 90 mmHg) and non-knee OA related mobility restrictions (neurological and musculoskeletal). All 46 participants were eligible for the study and they were scheduled for an initial assessment conducted in a university laboratory. Participants were recruited between March 2013 and October 2013. (For specific information about recruitment, please refer to Appendix F).

Upon arrival at the laboratory, participants were given a letter of information and consent form. Upon agreement to participate, their demographic data including height and weight, responses regarding their self-reported pain (VAS), data related to the functional tests, and isokinetic muscle strength testing were obtained. The performance-based tests used in this study were the 6 Minute Walk Test, Timed Up and Go test, and the stair climbing test, and a submaximal aerobic test (peak of oxygen consumption or VO₂peak) was the physiological test.

5.4 Outcome Measures

5.4.1 Isokinetic dynamometer system

All muscle strength tests were performed by the same study researcher using the isokinetic dynamometer Biodex System 3 Pro (Biodex Medical Systems, Shirley, NY, USA). The Biodex consists of a secure seat, a dynamometer with a T-base and an operation panel connected to a microcomputer [16]. The Biodex can be set at a constant velocity while accommodating resistance throughout a joint’s range of motion (ROM) [37]. This resistance is supplied using an electric servo-controlled mechanism at a user-defined constant velocity [17, 37]. Moreover, the Biodex software compensates for the effects of gravity as part of the setup with the subjects positioned appropriately. The software calculates the gravitational
correction values before each test by measuring the torque exerted on the dynamometer arm by the weight of the limb [16].

As recommended by the Biodex’s software manufacturer system and from studies that have previously used the isokinetic dynamometer Biodex System [16, 38, 39], all torque data were filtered with a 6 Hz low-pass filter (Butterworth, 6th order). This is an important feature applied to eliminate spike artifacts [16, 38]. It reduces the amplitude of any artifacts so higher frequencies are attenuated more and lower frequencies less [38]. Data were also windowed to reduce the possibility of selecting incorrect peak torque values for each repetition due to end range spike oscillations and artifact in the torque curve [18]. The reliability of windowed data for concentric knee flexion and extension has been reported to be .90 to .96 with Biodex systems [40].

5.4.2 Muscle strength measurement

Strength measurements were conducted for the affected knee or, in the case of bilateral knee OA, the most symptomatic knee. Participants were positioned in sitting with the back supported and the hips at an 85° angle. The trunk and thigh were stabilized with straps and the lower leg was secured to the lever arm with a padded cuff positioned just proximal to the medial malleolus. The approximate axis of the knee (through the lateral epicondyle of the femur) was aligned with the centre of the dynamometer’s axis of rotation. Prior to testing ROM was established from 90° angle of knee flexion to 0° angle of full knee extension. Concentric strength of the quadriceps muscle was measured at three different angular velocities of 60°/s, 90°/s and 120°/s. The order of all three pre-selected isokinetic angular velocities was randomized. The dynamometer’s data were sampled at 100 Hz based on manufacturer’s proprietary software.

Participants were allowed to practice, at each angular velocity and at a sub-maximal effort, 2 to 3 repetitions of concentric extension-flexion prior to the actual test. This practice was allowed to ensure familiarization with the test procedures. Then the protocol involved three sets of 5 maximal repetitions, and each set was performed under a pre-selected angular velocity. The peak torque from each set of 5
repetitions was used as the average isokinetic muscle strength of each pre-selected angular velocity. The participants were asked to apply as much force as they could in a consistent way during each repetition. Standardized verbal encouragements such as “push up hard” and “pull down hard” were given during the testing. Participants had a minimum of two minutes recovery between sets and then the test was repeated with a different angular velocity. Results from isokinetic muscle strength test were expressed in Newtons meters (N.m).

5.4.3 Obesity

Obesity is commonly measured by the individual’s Body Mass Index (BMI) which is the individual’s weight divided by his height. The standard categories for BMI include normal weight (18.5-24.9 kg/m²), overweight (25-29.9 kg/m²) and obese (30 kg/m² or more) [41]. The obesity category is divided into three subcategories: class I obesity (BMI 30-34.9 kg/m²), class II obesity (BMI 35-39.9 kg/m²), and class III obesity (BMI ≥ 40 kg/m²) [41].

5.4.4 Self-reported measurements

Pain was assessed using a Visual Analog Scale (VAS). The VAS is a measurement tool that indicates the amount of pain an individual experiences measured across a continuum of values [14]. The scoring range was from 0 (no pain) to 10 (highest pain level). The participants were asked to grade the amount of pain they experienced by indicating it on a horizontal line between 0 and 10. The VAS was used to record participants’ perceived level of pain before and after isokinetic muscle testing of the quadriceps was completed. The VAS has been validated for pain [42] and has been used in previous studies with individuals with knee OA [14, 43].

5.4.5 Imaging examination

The Kellgren-Lawrence scale (KL) method of radiographic examination [36] was used to score the severity of knee OA and to detect differences between groups. KL is the earliest and by far the most
commonly used global scale that gives an overall score of OA severity ranging from zero to four [36, 44]. The confirmation of several features were graded as an evidence of OA: grade 0, no radiographic findings of OA; grade 1, possible osteophytes and doubtful narrowing of joint space; grade 2, definite osteophytes and narrowing of joint space; grade 3, moderate multiple osteophytes and definite narrowing of joint space; and grade 4, large osteophytes and marked narrowing of joint space [36]. Both tibiofemoral compartments of the knee were assessed using a standard set of radiographs for reference [36].

5.4.6 Performance-based tests and physiological test

Three performance-based tests of physical functioning and one physiological test were obtained during a single testing session. The functional tests consisted of the Six Minute Walk Test (6MWT), the Timed Up and Go Test (TUG), and the modified Margaria stair climbing test [45]. Peak of oxygen consumption (VO₂peak), based on a nomogram previously used [46, 47] for calculation of upper body aerobic power with an arm ergometer, was the physiological test used.

The 6MWT is generally conducted in an enclosed, quiet corridor on a 25-meter track delineated by two lines marked on the floor [48]. Patients were instructed to walk from one line to the other, covering as much ground as possible in six minutes. Individuals were told that they could rest if they became too short of breath or tired, but to continue walking when they were able to do so. To calculate the walking distance, a metre wheel was used to measure the additional steps of any incomplete lap (in meters). The procedure for the TUG requires documenting the time, in seconds, that an individual takes to rise from a standard armchair, walk 3 meters, turn, walk back to the chair and sit down [49]. The participants were allowed to use any assistive devices that they would normally use for walking, to make them feel safe and comfortable during the test. Prior to testing, the subjects were warned that there would be two test trials and then they were instructed about the basic sequence of the test as follows: “When I say, ‘go’, you will stand up pushing from the arm of the chair, walk to the mark (line) on the floor, turn around, walk back to the chair and sit down. I will be timing you using a stopwatch.” The subjects were allowed to rest, as much as they needed, between each trial. The average of these two trials was used as
the final score. A shorter time taken to complete the task indicates a lower risk for falling and greater functional status.

Lower limb mechanical power output was assessed by a stair climbing test. This test is a modified version from the original test proposed by Margaria et al. [50] and has been previously validated in obese individuals [51-53]. Participants were asked to climb one step at time, at the highest speed possible. Even though they were allowed to use railings, they were encouraged to use them only if they felt it was extremely necessary. A staircase of 13 steps covering a total vertical distance of 2.0 meters was used. The final climbing time of the participants was obtained with a stop watch. The average mechanical power (W) can be calculated by multiplying body mass (BM), gravity (g) and vertical distance (h) and dividing its outcome by time (t).

The arm ergometry test was used to predict the VO$_2$peak in participants with knee OA. The participants were asked to pedal at a frequency of 70 revolutions per minute (rpm) against a constant workload of 21 Watts (125kg/min) for females and 42 Watts (250kg/min) for males. The workload was adjusted and maintained using the weights from the arm ergometer [47, 54]. To predict VO$_2$peak using an arm cycling submaximal test, the subjects should achieve a continuous steady state heart rate either equal to or above 110 beats per minute (bpm) during the last 30 seconds of submaximal test [47]. Heart rate was monitored constantly using a chest strap heart rate monitor and a digital watch set (Polar Electro, Inc Woodbury, NY) during the test. The test’s length of time was four minutes and pulse rate was recorded every 10 seconds during the last 30 seconds, between the third and fourth minutes. If the difference between the lowest and the highest pulse rate, recorded in the last 30 seconds of exercising, did not exceed 5bpm, a steady state heart rate was considered to be present [46, 47]. The average HR, from the steady state, was used to find a corresponding VO$_2$peak (L.min) on the nomogram. Further to that, VO$_2$peak was calculated in ml/kg/min based on the nomogram’s equation: \( VO_2\text{peak (L.min)} \times 1000 / Body\ Weight\ (BW) \). All of the participants reached at least 110bpm or more; consequently, a new test was not needed. However, if their heart rates had not reached at least 110bpm during the last 30 seconds of
testing, the workload would have been increased by 21 W (125 kg/min) and a new test would have been initiated.

### 5.5 Data Analysis

Data were analyzed using the Statistical Package for the Social Sciences version 21 (SPSS 21) and Microsoft Excel 2010. The alpha (α) level was set at \( p < 0.05 \). Results are presented as mean ± standard deviation (SD) unless otherwise specified.

#### 5.5.1 Manipulation checks and group composition analyses

Of the 31 participants diagnosed with knee OA, 15 were considered obese (BMI ≥ 30 kg/m²) and 16 were non-obese. Specifically, of the 16 non-obese participants, 9 were overweight (BMI= 25–29.9 kg/m²) and 7 were healthy weight (BMI= 18.5–24.9 kg/m²). A one-way ANOVA between overweight and healthy weight participants with knee OA demonstrated that they did not differ significantly on any demographic or main variables of interest, including radiographic examination findings (p’s > .05). Likewise, a chi-square analysis did not reveal any significant difference in gender (p > .05) between the overweight and healthy weight groups. Therefore, we combined the overweight and healthy weight groups into one group: the non-obese OA group. Radiographic examination was obtained from all 31 participants diagnosed with knee OA. A one-way ANOVA between the obese OA and non-obese OA groups was conducted to examine whether knee OA severity was significantly different between these two groups. The analysis indicated no significant differences between-groups on knee OA severity (p > .05). See Table 5.1.
## Table 5.1: Baseline Information / Group

<table>
<thead>
<tr>
<th>Baseline information / Group</th>
<th>Mean (SD)</th>
<th>Minimum</th>
<th>Maximum</th>
<th>F</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese OA</td>
<td>65.9 (8.3)</td>
<td>50</td>
<td>80</td>
<td>3.1</td>
<td>0.54</td>
</tr>
<tr>
<td>Non-obese OA</td>
<td>70.6 (5.9)</td>
<td>62</td>
<td>81</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>65.8 (3.0)</td>
<td>60</td>
<td>72</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese OA</td>
<td>39.0 (8.4)</td>
<td>29.3</td>
<td>62.1</td>
<td>26.2</td>
<td>0.000</td>
</tr>
<tr>
<td>Non-obese OA</td>
<td>27.0 (2.6)</td>
<td>23.4</td>
<td>28.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>26.8 (2.5)</td>
<td>23.4</td>
<td>28</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Body Weight</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese OA</td>
<td>104.3 (19)</td>
<td>70</td>
<td>143.7</td>
<td>18.5</td>
<td>0.000</td>
</tr>
<tr>
<td>Non-obese OA</td>
<td>76.8 (11.2)</td>
<td>62</td>
<td>82</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>77.2 (11.4)</td>
<td>60</td>
<td>85</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>X-Ray (KL)</strong></td>
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<td></td>
</tr>
<tr>
<td>Obese OA</td>
<td>3.3 (0.97)</td>
<td>2.0</td>
<td>4.0</td>
<td>0.056</td>
<td>0.48</td>
</tr>
<tr>
<td>Non-obese OA</td>
<td>3.3 (0.8)</td>
<td>2.0</td>
<td>4.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Stair Climbing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese OA</td>
<td>171.5 (66.1)</td>
<td>79.95</td>
<td>344.00</td>
<td>18.3</td>
<td>0.000</td>
</tr>
<tr>
<td>Non-obese OA</td>
<td>328 (114.6)</td>
<td>170.00</td>
<td>579.75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>386.6 (112.7)</td>
<td>216</td>
<td>636</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VO₂Peak</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese OA</td>
<td>15.6 (5.3)</td>
<td>8.36</td>
<td>28.47</td>
<td>22.8</td>
<td>0.000</td>
</tr>
<tr>
<td>Non-obese OA</td>
<td>27.6 (6.6)</td>
<td>14.28</td>
<td>36.56</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>29.0 (6.0)</td>
<td>18.3</td>
<td>38.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TUG</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese OA</td>
<td>11.0 (2.8)</td>
<td>6.65</td>
<td>18.94</td>
<td>34.5</td>
<td>0.000</td>
</tr>
<tr>
<td>Non-obese OA</td>
<td>7.7 (1.2)</td>
<td>5.17</td>
<td>9.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>5.5 (0.86)</td>
<td>4.5</td>
<td>7.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>6MinuteWalk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese OA</td>
<td>270.2 (109.4)</td>
<td>75.0</td>
<td>425.0</td>
<td>46.2</td>
<td>0.000</td>
</tr>
<tr>
<td>Non-obese OA</td>
<td>447.7 (65.6)</td>
<td>325.0</td>
<td>555.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>549.7 (58.0)</td>
<td>475.0</td>
<td>665.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Another one-way ANOVA between the obese OA and non-obese OA groups and healthy control group was conducted to examine whether OA groups were significantly different from healthy control groups as observed on table 5.1. The data from the control group were mainly used to compare to the data
obtained from obese OA and non-obese OA groups during the isokinetic muscle strength testing. A one-way ANOVA demonstrated that they did not differ significantly on age (p > .05), but as expected, the control group significantly differed from the obese OA group on BMI (p ≤ .0001) and weight (p ≤ .0001). However, no significant differences were observed between the non-obese OA and control groups. A chi-square analysis did not reveal any significant difference in gender (p > .05) among the obese OA, non-obese OA and control groups.

Further analyses between obese OA and non-obese OA groups indicated that body weight (F (1, 29) = 24.4; p ≤ .0001) and BMI (F (1, 29) = 28.8; p ≤ .0001) were significantly different between groups (Table 5.1). The results of the three performance-based tests (stairs climbing, 6MWT, and TUG) and the VO2peak (physiological test) were also compared between the obese OA and non-obese OA groups. Analyses indicated that the results from the stair climbing test (F (1, 29) = 21.3; p ≤ .0001), 6MWT (F (1, 29) = 30.5; p ≤ .0001), TUG (F (1, 29) = 18.4; p ≤ .0001), and the VO2peak (F (1, 29) = 30.5; p ≤ .0001) were significantly different between groups (Table 1), with the obese OA group showing significantly lower scores in all tests.

5.6 Results

In order to test our first hypothesis that significant differences in isokinetic muscular testing between obese and non-obese individuals with OA and healthy control participants were expected only at the angular velocity of 60°/s, three one-way ANOVAs were conducted. The ANOVAs examined whether the isokinetic peak torque of the quadriceps muscle among the three groups differed at each pre-selected angular velocity of 60°/s, 90°/s and 120°/s (Table 5.2). Results indicated that there was a statistically significant difference in isokinetic peak torque between groups at each angular velocity (F (2, 45) = 21.1; p < 0.001) at 60°/s, (F (2, 45) = 26; p < 0.001) at 90°/s and (F (2, 45) = 25.4; p < 0.001) at 120°/s. Post-hoc comparison analysis revealed that no significant differences between the obese OA and non-obese OA groups were observed at the angular velocities of 90°/s and 120°/s. However, at 60°/s post hoc analysis indicated that the isokinetic peak torque of each group was statistically significant different from
each other. The control group (172 ± 71.6) was significantly different (mean difference = 110.3; p < 0.001) from the obese OA group (61.8 ± 12) and significantly different (mean difference = 59.4; p = 0.003) from the non-obese OA group (112.7 ± 35.7). And the non-obese OA group was significantly different (mean difference = 50.9; p = 0.012) from the obese OA group.

<table>
<thead>
<tr>
<th>Angular velocities</th>
<th>groups</th>
<th>Mean (SD)</th>
<th>Min</th>
<th>Max</th>
<th>F</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>60°/s</td>
<td>Obese OA</td>
<td>61.8 (12)</td>
<td>40.3</td>
<td>77.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-obese OA</td>
<td>112.7 (35.7)</td>
<td>54.6</td>
<td>149.8</td>
<td>21.5</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>172 (71.6)</td>
<td>76.2</td>
<td>274.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90°/s</td>
<td>Obese OA</td>
<td>49.5 (18.2)</td>
<td>26.4</td>
<td>88.1</td>
<td>23.2</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>Non-obese OA</td>
<td>72.2 (24.9)</td>
<td>32.5</td>
<td>124.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>154.2 (66.9)</td>
<td>64.9</td>
<td>248.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>120°/s</td>
<td>Obese OA</td>
<td>51 (17.1)</td>
<td>24.3</td>
<td>86.6</td>
<td>23.4</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>Non-obese OA</td>
<td>73.5 (27)</td>
<td>35.3</td>
<td>106.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>129.7 (43.7)</td>
<td>58.7</td>
<td>181.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5.2: (SD) Standard deviation; Angular velocities during isokinetic muscular strength test were measured in degrees per second (°/s) and the average peak torque of each group (Nm), are indicated as the Mean values. All groups were compared at each angular velocity.

In order to test our second hypothesis that after isokinetic muscle testing there would be an increase in knee pain at the angular velocity of 60°/s and that both obese and non-obese individuals with knee OA would experience an increase in pain, three initial repeated measures ANOVA examined whether knee pain, as measured with the VAS, changed from before to after isokinetic muscle strength testing, at the angular velocities of 60°/s 90°/s and 120°/s. Results indicated that knee pain at the angular velocity of 60°/s significantly changed (F (1, 30) = 25; p < 0.0001) from before (mean = 2.87, SD = 1.52) to after (mean = 4.32, SD = 2.1). However, no significant change in pain was observed at the angular velocities of 90°/s and 120°/s. The other two repeated measures ANOVAs examined whether both obese and non-obese individuals with knee OA experienced an increase in knee pain after isokinetic muscle strength testing at the angular velocity of 60°/s. Results indicated that the ratings in the obese OA group
significantly changed \((F (1, 14) = 16; p = 0.001)\) from before \((\text{mean} = 3.8; \text{SD} = 1.13)\) to after \((\text{mean} = 5.8; \text{SD} = 1.9)\); ratings in the non-obese OA group also significantly changed \((F (1, 15) = 10.9; p = 0.005)\) from before \((\text{mean} = 1.92; \text{SD} = 1.2)\) to after \((\text{mean} = 2.9; \text{SD} = 0.98)\) (Figure 5.1).

![Figure 5.1: VAS at an angular velocity of 60°/s: 15 obese OA and 16 non-obese OA: Between groups: the obese OA group demonstrated significantly higher VAS than the non-obese OA group \(p \leq 0.0001\). Within group: VAS significantly change from time 1 to time 2 for both groups; obese OA (*), \(p \leq 0.0001\) and non-obese OA (**), \(p = 0.005\).](image)

In order to test our exploratory question as to whether muscle strength, as measured by the peak torque of isokinetic muscle strength of the quadriceps and BMI would predict performance-based tests of individuals with knee OA, we conducted stepwise regression analyses between performance-based tests and the peak torque of isokinetic muscle strength and BMI. Prior to the analyses, we ensured that there was no evidence of strong multicollinearity among the independent variables (all Pearson correlation coefficients \((r)\) were < 0.80) [55]. Four stepwise regressions were conducted. The first three explored whether peak torque and BMI would predict performance-based tests: the 6MWT, TUG, and the stair
climbing test, while the last one explored whether peak torque and BMI would predict results on the physiological test (VO₂peak). The regression analysis indicated that BMI alone explained a significant proportion of variance of the 6MWT, $R^2 = 64.8\%$, $F (1, 29) = 53.3; p < 0.0001$. Likewise, BMI alone also explained a significant proportion of the variance of the TUG, $R^2 = 62.3\%$, $F (1, 29) = 47.9; p < 0.0001$. However both isokinetic muscle strength and BMI explained a significant proportion of the variance in the stair climbing test, $R^2 = 44\%$, $F (1, 28) = 11; p < 0.0001$). With respect to the physiological test, only the BMI explained a significant proportion of the variance in VO₂peak, $R^2 = 63.3\%$, $F (1, 29) = 50; p < 0.0001$) (Table 5.3).

<table>
<thead>
<tr>
<th>Performance-based tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Six Minute Walk test</strong></td>
</tr>
<tr>
<td>BMI alone explained a significant proportion of variance of the 6MWT, $R^2 = 64.8%$, $F (1, 29) = 53.3; p &lt; .001$</td>
</tr>
<tr>
<td><strong>Timed Up and Go</strong></td>
</tr>
<tr>
<td>BMI alone explained a significant proportion of variance of the TUG test, $R^2 = 62.3%$, $F (1, 29) = 47.9; p &lt; .001$</td>
</tr>
<tr>
<td><strong>Stairs Climbing Test</strong></td>
</tr>
<tr>
<td>Isokinetic muscle strength and BMI explained a significant proportion of variance of the Stairs test, $R^2 = 44%$, $F (1, 29) = 11; p &lt; .001$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Submaximal aerobic test</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peak of Oxygen consumption</strong></td>
</tr>
<tr>
<td>BMI alone explained a significant proportion of variance of the VO₂peak, $R^2 = 63.3%$, $F (1, 29) = 50; p &lt; .001$</td>
</tr>
</tbody>
</table>

Table 5.3: Summary table of Stepwise regression analysis – Isokinetic muscle strength test and BMI were predictors of performance-based tests and submaximal aerobic test
5.7 Discussion

The results of the current study demonstrated that the isokinetic muscle strength of the quadriceps, represented as peak torque, was significantly different between the obese OA and non-obese OA groups and the healthy control group at all angular velocities of 60°/s, 90°/s and 120°/s, with the obese OA group demonstrating the lowest peak torque at all angular velocities (Table 5.2). However, after further statistical analysis it was observed that only at 60°/s did the isokinetic peak torque show a statistically significant difference between the obese and the non-obese individuals with knee OA. This finding suggests that among individuals with knee OA, obesity may be a good indicator of quadriceps muscle weakness, when quadriceps muscle weakness is assessed at the angular velocity of 60°/s, as observed in our study. Therefore, when measuring extensor isokinetic muscle strength in individuals with knee OA, it should be assessed at a lower angular velocity, such as 60°/s, rather than higher angular velocities (e.g., 90°/s and 120°/s). Further analyses indicated that knee pain significantly increased from before to after isokinetic muscle strength testing, but only at the angular velocity of 60°/s. In addition, when observing changes in pain within the obese OA and non-obese OA groups, it was observed that only at an angular velocity of 60°/s both groups experienced a significant increase in pain ratings after isokinetic muscle testing. These patterns of results indicate that after isokinetic quadriceps muscle testing assessed at lower angular velocities, such as 60°/s, both obese and non-obese individuals with knee OA may experience a significant increase in knee pain. Finally, it was observed that BMI alone explained the proportion of variance of the 6MWT, the TUG, and VO₂peak, while the proportion of variance of the stair climbing test was explained by both BMI and isokinetic peak torque. These results suggest that performance ability might be more impaired as a direct consequence of obesity rather than muscle weakness.
5.7.1 Assessment of quadriceps isokinetic muscular strength in individuals with knee OA at different angular velocities

Many studies have indicated that muscle weakness is commonly associated with knee OA [14, 17, 56], and multiple protocols have assessed muscle strength at different angular velocities [1, 7, 14, 17]. A previous study compared isokinetic knee muscle strength between patients with early knee OA and healthy individuals [14]. The authors found that the isokinetic muscle strength of the quadriceps was significantly lower in individuals with knee OA (at 60°/s and at 180°/s, p < 0.001 and at 240°/s, p = 0.01) compared to healthy individuals [14]. Even though two of the angular velocities used in our study were different, we also observed that the isokinetic muscle strength of the quadriceps was significantly lower in individuals with knee OA compared to healthy controls, at all angular velocities (Table 2). Diracoglu et al. also compared findings between those diagnosed with knee OA at stage I and II of disease severity, which was found to be significantly different at all angular velocities; however, their participants diagnosed with knee OA had a lower BMI (23.7 ± 5.3) than those in the current study. Obesity may have a significant effect on soft-tissue structures, such as tendon, fascia and cartilage; consequently, it may have an effect on musculoskeletal diseases, such as knee OA [7], as observed in our findings.

Another study [21] indicated that in women, body weight and quadriceps muscle strength assessed at the angular velocity of 60°/s were highly negatively correlated (r = -0.74, P = 0.003); therefore, the more obese the participant, the greater the reduction of quadriceps strength. On the other hand, no significant association between obesity and quadriceps muscle strength was observed in men [21]. Likewise, we found that, at 60°/s, a significant difference (p = 0.012) was observed between obese OA and non-obese OA groups (Table 2), but not at 90°/s or 120°/s. During isokinetic contraction, increased muscular output produces increased resistance rather than acceleration [16, 57]. It has been previously indicated that the muscular torque exerted during isokinetic testing is normally higher at lower angular velocity of movement [16]. Therefore, if at a lower angular velocity, such as at 60°/s, a higher muscular torque is produced, decreased muscle strength of obese and non-obese individuals with knee OA, measured at 60°/s may be more evident. This increase in torque may be attributed to different
neurological activation patterns of motor units at different velocities [16, 57]. Consequently, we suggest that to detect muscle weakness between obese and non-obese individuals with similar radiological diagnose of knee OA, a lower angular velocity should be used during isokinetic muscular testing.

5.7.2 Assessment of knee pain in individuals with knee OA at different angular velocities

Knee pain has been previously reported in the presence of muscle weakness [2, 17, 58-60]. In agreement, our study also indicated that knee pain in individuals with knee OA significantly increased (p <0.0001) after isokinetic muscular testing of the quadriceps at the angular velocity of 60°/s. As the individuals exert a higher muscular torque at a lower angular velocity, it is expected that pain to be further aggravated. At a lower velocity these individuals need to create a higher muscular torque in order to produce movement; consequently at this point they may be already working close to their maximal capacity, resulting in pain increase[1, 14, 16]. A previous study [61] compared the peak torque and functional status of individuals with knee OA with healthy controls. Different from our study, the authors used 90°/s as the lowest angular velocity and 150°/s as the highest angular velocity [61]. However, similar to our results, they found that the average pain levels from individuals with knee OA (3.05 ± 0.94) did not significantly change (p > 0.05) right after isokinetic muscle testing of the quadriceps at both angular velocities of 90°/s and 150°/s. O’Reilly et al. [2] observed the importance of quadriceps strength, structural change, and psychological status in terms of knee pain in 300 men and women with pain and 300 controls without pain. Even though muscle strength was measured with isometric muscle testing, the authors observed that participants with knee pain had lower voluntary quadriceps strength than those without pain (p < 0.005) [2]. Therefore, it is possible that at an early stage of disease severity it is pain, not necessarily muscle weakness, the primary limiting factor during functional tasks in individuals with knee OA.

A recent study [59] evaluated whether quadriceps weakness, measured at angular velocity of 60°/s predicted worsening of knee pain. The authors followed obese individuals for 5 years and found that lower quadriceps muscle strength, compared to self-reported pain at baseline and at 60 months
follow up, was significantly associated with an increased risk of knee pain worsening in women (P = 0.0052), but not in men [59]. Moreover, at baseline, men and women were not significantly different on BMI, and both groups were considered obese [59]. Compared to our obese OA group (comprised of men and women), who reached 61.8 Nm ± 12 of mean peak torque and experienced significant increase (p = 0.001) in knee pain after isokinetic muscle testing, the women’s group from the Glass et al. study [59] reached a similar peak torque of 67.5 Nm ± 25.1. Interestingly, when comparing between their women’s group and our non-obese OA group, the non-obese OA group reached a higher peak torque of 112.7 Nm ± 35.7, and yet, they experienced a significant increase (p = 0.005) in knee pain after the test. It is well-known that women have lower muscle strength [62, 63], have a higher chance of developing knee OA [64], and experience higher levels of pain compared to men with knee OA [65, 66]. Therefore, it is possible that when the groups were separated according to gender those aspects were enhanced in the Glass et al. study. In addition, it is possible that the finding of quadriceps muscle weakness predicting worsening knee pain in women but not in men may be driven by gender-specific differences in risk factors for worsening of knee pain in osteoarthritis.

Other studies use weight loss and resistance exercise training to improve muscle strength, decrease adverse joint loading [67], improve function, and reduce knee pain [67, 68]. A systematic review [69] examined the effectiveness of resistance training on knee pain in patients with knee OA. Sixteen of the 18 randomized controlled trials included a supervised exercise program. Resistance training included isometric, isotonic, and isokinetic exercises. The average muscle strength improvement was 17.4% and 56% of the studies reported a significant reduction in knee pain following resistance training [69].

Therefore, based on our study results, we suggest that in obese and non-obese individuals at a chronic stage of knee OA, an increase in knee pain may be an inherent factor triggered by quadriceps muscle activation in individuals with knee OA. Also, we conclude that knee pain may increase when it is assessed during an isokinetic muscle strength test at the angular velocity of 60°/s. While during high angular velocities the torque output decreases, at a lower angular velocity individuals need to apply
greater force and consequently the torque output increases [57]. This decline or increase in torque output has been attributed to different neurological activation patterns of motor units at different velocities. [14, 57]. Therefore at the angular velocity of 60°/s quadriceps muscle weakness of individuals with knee OA was better detected and pain was exacerbated, particularly in those who are obese and sedentary. It is expected that at 60°/s the quadriceps muscle of these individuals may be already working close to its maximal capacity, resulting in pain increase [16, 57]. Therefore, from a rehabilitation perspective, conservative treatment for individuals with knee OA should also include resistance training to improve extensor quadriceps strength. Increase muscle strength may protect the knee from adverse loading, improve performance and decrease pain, particularly in obese individuals with knee OA [11, 31].

5.7.3 Quadriceps muscle strength, BMI and performance-based tests

Patients with knee OA typically present with limited ability to complete functional tasks that require activation of the quadriceps muscle [14, 28, 69]. This limitation is normally attributed to quadriceps muscle weakness [14], measured during an isometric or isokinetic muscle strength test and compared to age- and sex-matched individuals with no history of OA or knee pain [25]. A previous study indicated that preoperative quadriceps muscle strength is a strong predictor of postoperative functional ability [70]. Mizner et al. tried to predict postoperative functional outcomes and bodily pain using a pre-operative quality of life questionnaire and knee range of motion however, the authors did not significantly predict any of the postoperative functional outcomes used in the study (p > 0.05). However, when preoperative quadriceps muscle strength was included as part of the analysis, bodily pain, range of motion, and preoperative muscle strength to predict post-operative functional outcomes, they accounted for 41% of the variance of the TUG and 54% of the variance of the stair climbing test [70].

A systematic review observed whether muscle impairment associated with knee OA would be the primary cause of functional limitation in patients with OA [69]. The authors concluded that individuals with knee OA have significant muscle impairments and that muscle impairments affect functional performance. We certainly agree that muscle impairments affect functional performance, however, based
on our findings when obesity is taking into account, it seems that performance ability might be more impaired as a direct consequence of obesity rather than muscle weakness (Table 5.3). When we compared the isokinetic peak torque between the obese and non-obese individuals with knee OA and control participants, we noticed that the isokinetic peak torque was significantly different at all angular velocities (Table 5.2). However, only at the lower angular velocity of 60°/s were the obese OA and the non-obese OA groups significantly different (p = 0.012) from each other. At a lower angular velocity, the muscular output is higher in order to move against resistance [16]. Therefore, the quadriceps muscle strength between obese OA and non-obese OA was not significantly different until a higher muscular output was required, suggesting that muscle weakness alone may not explain functional impairment, particularly in obese individuals with knee OA.

A previous study evaluated the relative contributions of psychosocial and mechanical variables to physical performance measures in people with knee OA. When the authors combined quadriceps muscles strength, BMI, self-efficacy pain, and self-efficacy function, they observed that these variables explained 62% of the variance of the 6MWT. They also observed that self-efficacy function, quadriceps muscle strength, and BMI explained 51.7% of the variance of the TUG. However, the participants from this study had a mean BMI of 28.6 kg/m², indicating that, as group, they were overweight. In our study, on the other hand, the obese individuals had a mean BMI of 39 kg/m² indicating that, together, they were classified as obese class II (BMI 35-39.9 kg/m²) [41]. Consequently, when we used both extensor muscle strength and BMI to predict the 6MWT, TUG, VO₂peak and stair climbing test, we observed that BMI alone explained a significant proportion (p ≤ 0.0001) of the variance: 64.8% of the 6MWT, 62.3% of the TUG, and 63.3% of VO₂peak. The quadriceps muscle strength and BMI together explained a significant (p ≤ 0.0001) proportion of the variance of 44% of the stair climbing test. These findings indicate that, for individuals with knee OA, quadriceps muscle weakness may contribute to explain functional limitations; however, when obesity is present, it seems to play a more substantial role in explaining impaired functional capacity as compared to quadriceps muscle weakness. Moreover, obesity is an increasingly common disorder, particularly among individuals with knee OA [64, 71]; therefore, we suggest that
obesity may be a good predictor of impaired function, and therefore treatment targeting weight loss and muscle strength training are crucial to improve functional capacity of obese individuals with knee OA.

5.8 Limitations, future directions, and conclusions

Recruitment in order to increase our sample size was challenging for a variety of reasons, such as recruiting patients within a BMI category of 18.5-24.9 kg/m². However, we obtained important findings with significant impact and relevance to the clinical setting. Future research should also measure the impact of body weight loss and improvement in extensor muscle strength on functional capacity of individuals with knee OA before and after total knee replacement surgery.

In conclusion, we observed that muscle weakness and knee pain were better detected between obese and non-obese individuals with knee OA when measured at an angular velocity of 60°/s. Therefore, when measuring extensor isokinetic muscle strength in individuals with knee OA, if possible, it should be assessed at an angular velocity of 60°/s, rather than higher angular velocities, such as 90°/s and 120°/s. Moreover, performance-based tests might be more impaired as a direct consequence of obesity rather than muscle weakness. Therefore, clinicians should encourage obese patients with knee OA to lose weight and those who are not obese to maintain a healthy weight.
5.9 References


Chapter 6

General Discussion and Future Perspectives

6.1 Thesis Overview

The World Health Organization (WHO) estimates that worldwide 9.6% of men and 18% of women older than 60 years of age have symptomatic OA [1]. WHO also estimates that 80% of those with OA will have limitations in movement, and 25% cannot perform their major daily activities of life [1]. Approximately 3 million Canadians (1 in 10) have OA and it is estimated that 85% of Canadians will have been diagnosed with OA by the age of 70 years [2, 3]. In 2010, approximately 49% of seniors over the age of 65 years were living with symptomatic OA [4, 5]. By 2040, this number is expected to increase to 71%.

However, the effects of OA tend to be worse in obese individuals [6, 7]. The onset of OA in weight-bearing joints such as knees and hips has been associated with obesity [8, 9]. In 2001, the total cost in health care for obesity was about $1.6 billion, which corresponds to 2.2% of the total health care expenditures for all diseases in Canada [6]. The Canadian Community Health Survey (CCHS) in 2004 indicated that the combined number of overweight and obese adult people was about 59.1% [10].

Previous studies have made many suggestions to improve the quality of life of obese people with knee OA. There are many conservative treatments, diets and exercise therapy [11-15] or surgical procedures for joint replacement [16-18] and weight loss [19]. However, it is important to assess patients’ self-perception of disability in a consistent way, as well as their level of physical activity before prescribing general exercise therapy, diets, or prioritizing surgical treatments.

Further information on how those individuals perceive their own level of disability, based on their ability to perform functional tasks, is needed. Consequently, health care providers lack the ability to develop better treatment plans that suit each patient, based on their needs. Moreover, evidence suggests
that the psychological aspect of the disability of obese individuals with knee OA should be further explored as part of research protocols and conservative treatments [20-23]. Additionally, quadriceps muscle weakness is normally found in individuals with knee OA [24], and it is considered an important factor in physical disability and pain in these individuals [25]. In obese and non-obese individuals with knee OA, the literature discussing differences in muscle strength is limited. However, for rehabilitation professionals, it is important to understand the nature and extent of muscle weakness in these individuals, in order to recognize functional limitations and to possibly develop strategic, individualized treatment plans that are suitable for individuals, taking in to account their morphology. Therefore it is also important to identify whether quadriceps muscle strength differs between obese and non-obese individuals with knee OA in order to determine if this is a factor for consideration when developing a treatment plan.

The intent of this thesis was to advance understanding in the field of knee OA when associated with obesity, based on participants’ self-reported disability and biomechanical findings. This thesis aims to investigate whether self-reported disability should be obtained before or after performance-based tests, to explore changes in self-reported disability, knee pain associated with depressive symptoms and knee muscle strength in obese and non-obese individuals with knee OA.

6.2 Relevance of findings from Chapter 3

6.2.1 Measuring self-reported disability before and after performance-based tests in individuals with osteoarthritis of the knee.

In Chapter 3 of this thesis our study showed that self-reported disability, measured by the WOMAC questionnaire, was significantly higher after as compared to before the completion of performance-based, functional tests. These results suggest that the WOMAC questionnaire, when possible, should be administered to individuals with knee OA after performance-based tests because it captures participants’ experience of physical limitations in real time. Significant differences were also observed between obese individuals and non-obese individuals with knee OA on all WOMAC scores,
with the obese individuals demonstrating higher scores for disability. In addition, when comparing the obese to the non-obese group, the non-obese OA group did not show any significant change in WOMAC scores from before to after performance-based tests, whereas all scores from the obese OA group changed significantly from before to after.

It has been previously reported that WOMAC total scores ranging from 23 to 33 or higher than 33 are suggestive of high disability levels [26]. Our obese OA group had an average score of 48.4 for the WOMAC total before performance-based tests. This number increased significantly (p < .0001) to 66.6 after performance-based tests were completed. This high score suggests high disability levels and this increase in self-reported disability after performance-based tests indicate that our obese participants had a more realistic perception of their physical limitations once they engaged in related physical activity tasks, suggesting that relying on self-reported disability alone may lead to an overestimation of one’s abilities, especially for an obese population with knee OA.

While there is no standardized recommendation as to whether measures of self-reported disability should be obtained before or after performance-based tests in individuals with knee OA, some researchers avoid obtaining self-reported disability measures after performance-based tests in order to avoid the influence that these tests may have on participants’ answers [27]. However, on a daily basis we all face physical tasks that require basic functional abilities. Performance-based tests represent the ability to perform activities, rather than the perceived experience of performing them, as would be measured by a questionnaire [28, 29]. Therefore, it seems logical that a more accurate self-reported disability score will be obtained after a functional task is completed. Following the most recent recommendation from the literature that performance-based tests of physical functioning (e.g., stair-climbing test, TUG, 6-MWT) should be used as complementary assessment tools to self-reported measures [30], we applied these tests in our two groups of individuals with knee OA with the aim of determining that self-reported disability obtained after performance-based tests would capture participants’ experience of physical limitations more accurately.
Our results also indicated that physical activity and BMI explained a significant proportion of variance of self-reported disability, particularly after performance-based tests were completed. These results indicate that physical activity and BMI accounted for greater variability in self-reported disability scores from individuals with knee OA. Many obese individuals who report having knee pain or who have been diagnosed with knee OA avoid physical activities and consequently they become more physically disabled [13, 31, 32]. On the other hand, participating in physical activity and losing weight are important factors in decreasing disability and improving knee pain [11, 12, 33, 34]. Therefore, future studies should explore specific treatment plans that include increase in physical activities and exercise based on self-reported disability scores and physical limitations as a result of OA and obesity. Conservative treatment plans including, diet and exercise for obese individual with knee OA should be prioritized, rather than TKR surgery. However, this treatment plan should accommodate these individuals to a level that is equivalent to their actual capacity to exercise.

6.3 Relevance of findings from Chapter 4

6.3.1 Measuring knee pain before and after performance-based tests in obese and non-obese individuals with osteoarthritis of knee

Knee pain is probably the most remarkable symptom in OA [35, 36] and it is likely the most debilitating aspect of this disease [20, 37]. The effect of pain during daily activities is the main reason individuals with knee OA seek for conservative or surgical treatment [16]. According to the literature, radiological confirmation of severe OA and knee pain followed by decrease in functional performance are the most common reasons surgeons recommend total knee arthroplasty [16, 38]. However, radiographic findings show poor correlations with knee pain [39-42]. Previous studies have reported several cases of people with structural changes, based on radiological information, who indicate mild or no pain [39-42], whereas others with higher levels of joint pain may not have severe radiographic indices of OA [43]. These conflicting findings raise questions about the nature of knee pain which seems to vary among individuals diagnosed with knee OA [40, 44].
In Chapter 4 of this thesis our study indicated that self-reported pain scores were significantly higher after as compared to before the completion of performance-based tests. In a study comparing pain due to knee OA in women and men [45], the authors found no significant (p = 0.08) difference between women and men at rest, but during a gait speed test women had a significantly higher (p = 0.04) level of pain (7.34 ± 5.69) compared to men (5.69 ± 4.95). Suggesting that after daily activities such as going up or down stairs, walking long distances or standing from a sitting position, the levels of knee pain tend to increase and the experience of pain lived by each individuals may be expressed differently.

When our sample was divided into obese and non-obese individuals with knee OA, we observed that the obese group demonstrated significantly higher levels of self-reported pain. The Visual Analog Scale (VAS) ratings captured a significant increase in pain in both groups from before to after performance-based tests. The WOMAC pain subscale, on the other hand, only captured change in the obese OA group after completion of performance-based tests. Even though the WOMAC pain score and the VAS ratings are reliable tools to measure pain in individuals with knee OA [46], the way in which the experience of pain is captured, by each measurement, may influence its final outcome [47]. However, there are no previous studies indicating whether one method of pain measurement is preferable over another when evaluating knee pain in individuals with knee OA. Yet, there is evidence demonstrating that the WOMAC subscales of pain and physical function are more influenced by the ability to perform activity than by the patients’ experience of pain and their perception of difficulty of performing daily activities [48, 49]. Moreover, knee pain typically increases during functional activities as a “momentary physical experience”. Therefore, it seems logical to capture the experience of pain at the moment of its occurrence, as measured with the VAS rating, rather than few minutes later (as measured with the WOMAC pain subscale), when some of that physical experience had decreased.

Furthermore, the non-obese OA group was capable of performing functional activities significantly better with significantly less pain than those in the obese OA group therefore; we did not expect significant changes on the WOMAC pain subscale for the non-obese OA group. Consequently, we may suggest that the VAS pain rating may be a better tool for assessing knee pain of individuals
diagnosed with knee OA during or right after performance-based tests, because it captures the pain at the moment of its occurrence.

It is well-known that depressive symptoms may affect knee pain and subsequently function [20, 47]. Our obese OA group showed higher levels of depressive symptoms and consequently higher levels of pain. Therefore, it was not a surprise that a significant proportion of variance $R^2 = 35.7\%$ ($p < .0001$) of the WOMAC pain, which only captured change in the obese OA group after functional tests, was explained by depressive symptoms. While, both depressive symptoms and BMI explained a significant proportion of the variance of the VAS ratings, $R^2 = 52.6\%$ ($p < .0001$) after performance-based tests. Even though, we cannot suggest that higher levels of depressive symptoms can directly interfere with functional capacity of obese individuals with knee OA, we may speculate that, indirectly, depressive symptoms seem to affect their willingness to becoming more physically active.

The findings from this study also demonstrate that depressive symptoms and BMI accounted for 49% of variance on the physical component of quality of life (QoL) in patients with knee OA. However, only BMI accounted for 23% of the variance on the mental component of QoL. In terms of perceived need for surgery (PNS), both depressive symptoms, as measured by BDI-II scores, and BMI explained a significant proportion of variance of PNS, $R^2 = 55\%$ ($p < .0000$), indicating that depressive symptoms and BMI accounted for 55% of variance of a patient’s perceived need for surgery.

Therefore, researchers and clinicians may need to consider the role of depression in perceived pain, functional performance, quality of life and perceived need for surgery as a key factor when developing treatment plans and to further engage obese people with knee OA in physical activities. Future investigations should also focus on treatment for depression with weight loss therapy to try determining whether a combination of treatments is more effective than treating obesity or depressive symptoms separately. Because pain and depression also seem to be relevant factors affecting the quality of life of obese individuals with knee OA. It would also be important to increase the sample size in order to have a better representation of this population. Moreover, longitudinal studies are warranted to measure the
impact of reduction in depressive symptoms or body weight on the experience of pain due to knee OA, QoL, and level of physical activity before and after total knee replacement surgery.

6.4 Relevance of findings from Chapter 5

6.4.1 Knee pain and isokinetic quadriceps muscle strength in knee osteoarthritis

Quadriceps strength declines with age, and aging is a risk factor for the development and progression of knee osteoarthritis (OA) [25, 50, 51]. Quadriceps muscle weakness is also considered an important factor in physical disability and pain in individuals with knee OA [25]. However, despite evidence that obesity may affect soft tissues, such as muscles and tendons [52-54], the majority of studies have focused on the impact of obesity on bone and joint disorders such as fractures and joint malalignment [55, 56]. Therefore, it is important to assess whether knee extensor muscle weakness, and the experience of pain associated with it, affect both obese and non-obese individuals with knee OA.

Isokinetic dynamometry provides a safe and effective method of assessing muscle strength by assessing dynamic, or isokinetic, muscular contractions through a defined range at a constant velocity. From a review of the literature pertaining to muscle strength testing in persons with knee OA, we found that the most common isokinetic testing velocities reported were 60°/s, 90°/s and 120°/s [50, 57-59]. Therefore our main objective was to examine whether the results from isokinetic muscular testing of the quadriceps would differ between obese and non-obese individuals with knee OA, as well as between all those with OA and a control group, using the most common angular velocities previously reported.

However, conflicting findings were observed during quadriceps muscle strength testing when body weight is taken into consideration for individuals with knee OA [60, 61]. While a previous study [60] indicated that, among the 13 women diagnosed with OA, there was a strong, highly significant negative correlation between body weight and extensor strength ($r = -0.74$, $P = 0.003$), a more recent study [61] indicated that peak quadriceps strength did not significantly differ by BMI groups or by the presence of knee OA. Therefore, the relationship between obesity and lower extremity muscle strength needs to be further explored.
In Chapter 5 of this thesis our results demonstrated that the isokinetic muscle strength of the quadriceps, represented as peak torque, was significantly different between obese and non-obese individuals with knee OA and compared to a healthy control group at all angular velocities of 60°/s, 90°/s and 120°/s, with the obese OA group demonstrating the lowest peak torque at all angular velocities. However, it was only at 60°/s that the isokinetic peak torque showed a statistically significant difference between the obese and the non-obese individuals with knee OA. A muscular torque exerted during isokinetic testing decreases with increasing angular velocity of movement [62], while at a lower angular velocity individuals need to apply greater force and consequently the torque output increases [63]. This decline or increase in torque output has been attributed to different neurological activation patterns of motor units at different velocities [24, 63]. In individuals with knee OA the quadriceps muscle commonly shows decreased strength [24, 50]. Therefore, when the quadriceps muscle of these individuals is assessed at the angular velocity of 60°/s, significant differences between obese and non-obese individuals with knee OA became evident.

Given that arthritic knees are often stiff and painful [64, 65] and that strength measures may produce or increase pain momentarily during test movements [24], our second objective was to examine whether knee pain, measured with the visual analogue scale (VAS), would change after isokinetic muscle strength testing, at the angular velocities of 60°/s, 90°/s and 120°/s, and whether such change would be experienced by both obese and non-obese individuals with knee OA. A Previous study [66] tried to compare the peak torque and functional status of individuals with knee OA with healthy controls using higher angular velocities. They found that the average pain levels from individuals with knee OA (3.05 ± 0.94) did not significantly change (p > 0.05) right after isokinetic muscle testing of the quadriceps at both angular velocities of 90°/s and 150°/s. Suggesting that in order to observe increase in knee pain, extensor isokinetic muscle strength in individuals with knee OA should be assessed at a lower angular velocity, such as 60°/s, rather than higher angular velocities (e.g., 90°/s and 120°/s). Our results indicated that knee pain significantly increased from before to after isokinetic muscle strength testing, but only at the angular velocity of 60°/s. In addition, when observing changes in pain within the obese OA and non-obese OA
groups, it was observed that only at the angular velocity of 60°/s did both groups experience a significant increase in pain ratings after isokinetic muscle testing. It is expected that at 60°/s (lower angular velocity) the quadriceps muscle of these individuals may be already working close to its maximal capacity, resulting in pain increase [62, 63]. Therefore, based on our study results, we suggest that an increase in knee pain may be an inherent factor triggered by high quadriceps muscle activation in individuals with knee OA.

In terms of muscle strength and its relation to functional tests, it is interesting to highlight that the peak torque from obese and non-obese individuals with knee OA only explained a significant proportion of the variance in the stair climbing test [67, 68]. On the other hand, BMI was the main predictor in all other performance-based tests including the 6MWT and stair climbing test and the physiological test of VO$_2$peak. In summary, the isokinetic muscle strength from obese and non-obese individuals with knee OA only differs at the angular velocity of 60°/s, when the quadriceps muscle of these individuals may be already working close to its maximal capacity against an increased resistance proportional to the torque produced during muscle contraction [62, 69]. Moreover, the peak torque from obese and non-obese individuals with knee OA poorly predicted performance-based tests. Consequently, performance ability might be more impaired as a direct consequence of obesity rather than muscle weakness.

Knee pain as a result of isokinetic muscle testing was only significantly different between obese and non-obese OA individuals at the angular velocity of 60°/s. Not a surprise considering that the experience of pain, under functional testing, seems to be intrinsically related to the amount and intensity of activity sedentary obese individuals with knee OA perform. Therefore, at higher angular velocities the muscular torque exerted during isokinetic testing tends to be lower, which may not aggravate pain to the point where it could be differentiated between obese and non-obese individuals with knee OA. In addition, sedentary obese individuals with knee OA tend to adapt to their pain and disability by performing lighter physical activities [20, 23, 70-72].
Future research should measure the impact of body weight loss and improvement in extensor muscle strength on functional capacity of individuals with knee OA before and after total knee replacement surgery.

6.5 Limitations

1. The data from all three studies in these theses were obtained from the same sample of individuals with knee OA. Despite support from the department of orthopedic surgery, participants were recruited from a case load of one orthopedic surgeon only. Therefore, recruitment was challenging in terms of patient resources.

2. Recruiting patients diagnosed with knee OA and within a BMI category of 18.5-24.9 kg/m² was also very challenging and nearly impossible due to our limited resources. We noticed that the majority of patients who were on a consultation list with a surgeon were slightly overweight, overweight or obese. Therefore we were not able to have a comparison group of those with low body weight who required TKR surgery. However, this also may be an indicator that body weight is a key factor in relation to the disability associated with OA.

6.6 Final Remarks

Both obesity and knee osteoarthritis are rapidly becoming significant and costly health concerns in Canada. The impact of these conditions on society, and their relationship to one another, is important to investigate in terms of public health, health policy and individual health status. TKR surgery is one of the fastest growing elective surgeries in Canada, and ways to delay or prevent it are critical. When considering those who require TKR surgery, it is important to elucidate key factors in their management that can help with conservative therapy both pre- and post-operatively. First and foremost, when determining their level of disability, using the most appropriate tests in the most appropriate sequence is critical. In this study we were able to demonstrate that self-report measures of disability, such as the
WOMAC, are better done following functional tests, such as the 6MWT, TUG and stair-climbing, so the individual has a realistic impression of their abilities. This is particularly true of those with higher BMIs, and lower levels of self-reported physical activity, since both of these variables predict a significant proportion of variation in WOMAC scores, especially following functional testing.

We were also able to demonstrate that while the WOMAC pain subscale gives a general impression of pain, the VAS measured immediately following functional tests, gives a much better idea of the level of pain associated with activity. The VAS is easy to administer and not time consuming, and should be used as a complement to the WOMAC as it is more sensitive to pain levels at the moment rather than over time.

Assessing depressive symptoms is another critical measurement for those who are both obese and who suffer from knee OA. In this study we demonstrated that depressive symptoms contributed significantly to pain levels, quality of life and perceived need for surgery in those with knee OA. The differences were especially significant for those who were obese. These findings suggest that a measure of depression should be done when assessing pain and function of obese individuals with knee OA, and that managing these symptoms would be critical in any treatment plan.

The final portion of our study sought to examine the role of quadriceps strength in those with knee OA compared to controls, and in those with knee OA who were obese and those who were normal weight. While we found that those with knee OA were weaker than controls at all velocities of isokinetic testing, and that one measurement in particular distinguished between those who were obese and those who were not, BMI remains the strongest predictor of disability when it comes to most functional tests. With the exception of stair climbing, which arguably relies on gravity more than the other tests, obesity was still more debilitating with knee OA than was decreased quadriceps strength.

In conclusion, when assessing those with knee OA who are obese, it is important to do self-report tests following functional tests, the VAS should be used alongside the WOMAC when doing functional tests as it gives a real time impression of pain, and depressive symptoms should also be measured. All of the functional and self-report tests used in this thesis are easily administered clinically. The self-report
tests include the WOMAC, the VAS, the Physical Activity Questionnaire, and the BDI II; the functional tests include the 6MWT, the TUG, and the stair climbing test. The more complex test of assessing VO\textsubscript{2} peak, and isokinetic muscle strength, while useful for the purposes of this thesis, are time consuming, require specialized equipment, and are not always possible in a clinical setting, however, they would also not be necessary clinically to determine level of disability of obese individuals with knee OA. The simple tests done in this thesis, in the order determined, could ensure that obese individuals with knee OA get an appropriate, tailored treatment plan whether they require TKR surgery or not.

The studies in this thesis have answered some questions related to self-report measurements, the influence of depressive symptoms in self-reported pain and whether knee pain and quadriceps muscle strength differ between obese and non-obese individuals with knee OA. These studies have also generated directions for further exploration in knee OA and obesity research. In particular, investigations of conservative interventions and treatments, which could have a potential disease-modifying effect and delay in functional decline that are urgently needed, in view of the enormous impact of knee OA and obesity in society. It is hoped that the results of this thesis can guide surgeons, therapists and other health care practitioners in making appropriate clinical decisions with respect to the testing and treatment of those with knee OA, particularly those who are also obese.
6.7 References


Appendix A

QUEEN’S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS RESEARCH ETHICS BOARD-DELEGATED REVIEW

April 05, 2012

Dr. Alice Aiken
School of Rehabilitation Therapy
Louise D. Acton Building
Queen’s University

Dear Dr. Aiken

Study Title: REH-512-12 Perceived level of disability in obese individuals with osteoarthritis of the knee
File # 6006698
Co-Investigators: Mr. K. Da Silva, Dr. Mark Harrison

I am writing to acknowledge receipt of your recent ethics submission. We have examined the protocol, study design and methodology, Short Form Health Survey (SF-36), WOMAC Osteoarthritis Index LR3.1 (1R), Beck Depression Inventory (BDI), Assessment Sheet and the revised letter of information consent form for your project (as stated above) and consider it to be ethically acceptable. This approval is valid for one year from the date of the Chair’s signature below. This approval will be reported to the Research Ethics Board. Please attend carefully to the following listing of ethics requirements you must fulfill over the course of your study:

Reporting of Amendments: If there are any changes to your study (e.g. consent, protocol, study procedures, etc.), you must submit an amendment to the Research Ethics Board for approval. Please use event form: HSREB Multi-Use Amendment/Full Board Renewal Form associated with your post review file # 6006698 in your Researcher Portal (https://eservices.queenston.ca/romeo_researcher)

Reporting of Serious Adverse Events: Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other serious adverse events must be reported within 15 days after becoming aware of the information. Serious Adverse Event forms are located with your post-review file 6006698 in your Researcher Portal (https://eservices.queenston.ca/romeo_researcher)

Reporting of Complaints: Any complaints made by participants or persons acting on behalf of participants must be reported to the Research Ethics Board within 7 days of becoming aware of the complaint. Note: All documents supplied to participants must have the contact information for the Research Ethics Board.

Annual Renewal: Prior to the expiration of your approval (which is one year from the date of the Chair’s signature below), you will be reminded to submit your renewal form along with any new changes or amendments you wish to make to your study. If there have been no major changes to your protocol, your approval may be renewed for another year.

Yours sincerely,

[Signature]

Chair, Research Ethics Board
April 05, 2012

Investigators please note that if your trial is registered by the sponsor, you must take responsibility to ensure that the registration information is accurate and complete
QUEEN'S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS RESEARCH ETHICS BOARD

The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards and operates in compliance with the Tri-Council Policy Statement: Part C Division 5 of the Food and Drug Regulations, OHRP, and U.S DHHS Code of Federal Regulations Title 45, Part 46 and carries out its functions in a manner consistent with Good Clinical Practices.

Federalwide Assurance Number: #FWA00004184, #IRB00001173

Current 2012 membership of the Queen's University Health Sciences & Affiliated Teaching Hospitals Research Ethics Board:

Dr. A.F. Clark, Emeritus Professor, Department of Biochemistry, Faculty of Health Sciences, Queen's University (Chair)

Dr. H. Abdollah, Professor, Department of Medicine, Queen's University

Dr. R. Brison, Professor, Department of Emergency Medicine, Queen's University

Dr. M. Evans, Community Member

Dr. S. Horgan, Manager, Program Evaluation & Health Services Development, Geriatric Psychiatry Service, Providence Care, Mental Health Services, Assistant Professor, Department of Psychiatry

Ms. J. Hudaiein, Community Member

Mr. D. McNaughton, Community Member

Ms. P. Newman, Pharmacist, Clinical Care Specialist and Clinical Lead, Quality and Safety, Pharmacy Services, Kingston General Hospital

Dr. W. Race, Emeritus Professor, Department of Pharmacology & Toxicology, Queen's University

Ms. S. Rohland, Privacy Officer, ICES-Queen's Health Services Research Facility, Research Associate, Division of Cancer Care and Epidemiology, Queen's Cancer Research Institute

Dr. B. Simchinson, Assistant Professor, Department of Anesthesiology and Perioperative Medicine, Queen's University

Dr. A.N. Singh, WHO Professor in Psychosomatic Medicine and Psychopharmacology
Professor of Psychiatry and Pharmacology, Chair and Head, Division of Psychopharmacology, Queen's University, Director & Chief of Psychiatry, Academic Unit, Quinte Health Care, Belleville General Hospital

Dr. E. Tsak, Associate Professor, Department of Pediatrics and Office of Bioethics, Queen's University

Dr. E. VanDenKerkhof, Professor, School of Nursing and Department of Anesthesiology and Perioperative Medicine, Queen's University
Appendix B

THE EFFECT OF OBESITY IN SELF-REPORTED DISABILITY, KNEE PAIN AND ISOKINETIC QUADRICEPS STRENGTH IN KNEE OSTEOARTHRITIS

School of Rehabilitation Therapy – Queens’ University

Assessment Sheet

Code number __________  Assessment Date __________

Participants’ characteristics

Gender: Male / Female  Married status: Single □
Age Gender: __________  Married □
DOB: _________________  Live with partner □

Anthropometric Measurements

A. Height _______ m  Widow □
B. Weight _______ kg  Divorced □
C. BMI: ____________ Kg/m^2
D. Waist Circumference (WC): ___________ Neck Circumference: _________________
E. Hip Circumference: ___________ Wrist Circumference: _________________
F. Waist/Hip ratio: ___________ Thigh Circumference: ___________ Calf Circ.: ___________

Body Composition: Bioimpedance Analysis

G. Body fat%: __________
H. Visceral fat%: __________
I. Lean mass%: __________
J. Resting metabolism: _______________
K. Body Age: __________
Perceived Need for Surgery

L. Knee Joint Side______________

Perceived Need for Surgery
Do you think you need a Total Knee Replacement surgery?
The lowest possible response is zero (0) and it indicates no need for TKR surgery. On the other hand the highest possible response is ten (10) and it indicates the highest need for TKR surgery. Please indicate with a mark, at what level is your perception of surgery.

PNS / 10 ____________

0_______________________________________________10

Weight Satisfaction survey

M. Are you happy with your current weight?
□ yes □ no

N. If I ask you to self evaluate your weight category, how would you classify yourself?
□ Healthy weight □ Overweight □ Obese

O. Have you tried any diet before?
□ yes □ no

P. Have you joined any exercise program to improve your fitness level?
□ yes □ no

Q. Do you feel that your weight directly affect the amount of tasks you do in regular day?
□ yes □ no
Pain management

Pain Medication:
NSAIDS □ Acetaminophen □
Celebrex □ Aspirin □
Ibuprofen □ Other □ __________________________ □ Do not take meds
Supplements □ type: ___________________________
Glucosamine □ MSM □ Shark Cartilage □ Chondroitin □

Pain in other Joints:

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Visual Analog Scale pain

The extreme levels of pain are zero (0) “no pain at all” and ten (10) “my pain is as bad as it could possibly be”. Please indicate with a mark, at what level is your perception of pain.

0_______________________________________________10
Health Behaviors/Status

Smoking habits

Have you ever smoked cigarettes?

□ No

□ Yes,

If yes, do you still smoke? □ Yes or □ No

□ On average, how many packs per day have you smoked? ______ Packs

*Please check the box that best approximates to your daily level of physical activity

- Walking:
  □ walking slowly around the house/office/one block (< 3 METs)
  □ walking at a very brisk pace (3 - 6 METs)
  □ Jogging or running, hiking at moderate pace (> 6 METs)

- Household and occupation:
  □ Computer work at the desk, light hand tools, light house work activities (< 3 METs)
  □ Heavy cleaning, washing windows, carpet cleaning, mowing lawn (3 - 6 METs)
  □ Shovelling snow, carrying heavy loads (bricks or wood), farming, digging (> 6 METs)

- Leisure time and sports:
  □ Arts & crafts, playing cards, darts, fishing, playing instruments, croquet (< 3 METs)
  □ Bicycling light effort, dancing (ballroom slow/fast), Golf walking swimming (3 - 6 METs)
  □ Basketball game, Bicycling (moderate to heavy gear), cross country, soccer (> 6 METs)

Health status

I. In the PAST 6 MONTHS did you CUT DOWN or LIMIT your usual non-employment (including housework, school) or employment activities BECAUSE OF ARTHRITIS?

□ Yes / □ No

If yes, how many days? __________ Was it due to your arthritis? □ Yes / □ No

II. In the PAST 6 MONTHS were you COMPLETELY UNABLE to carry out your usual non-employment or employment activities BECAUSE OF YOUR ARTHRITIS?

□ Yes / □ No

If yes, how many days? __________ Was it due to your arthritis? □ Yes / □ No

* Med Sci. Sports Exerc. 2000;32(suppl.):S498-
Physical and Physiological Tests

Power output (Stair Climbing Test) Power can be obtained by $W=MB\cdot g \cdot h/t$
(Mb) Body Mass, (g) gravity = 9.8m/s, (h) vertical distance in meters and (t) time

Time to complete the task: _________(s)

Average pain /10_______
RPE: _________

Submaximal oxygen consumption/ Arm-ergometer

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<th>3 min 50 sec</th>
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Predicted VO2max: _____________l/min/kg

RPE: _________

Walking Test

**TUG test**

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<th>Trial 2</th>
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TUG: average: _______
Average pain /10_______
RPE: _________
Six Minute Walk Test

1 2 3 4 5 6 7 8 9 10 11 12 13
14 15 16 17 18 19 20 21 22 23 24 25 26
27 28 29 30 31 32 33 34 35 36 37 39 40

Distance walked________ m Pain /10______________
Extra Steps____________ m RPE: _____________

Muscle Strength Test

Strength test / Biodex ISOKINETIC 60°/s
ROM peak torque
| Knee extension 1 |   |
| Knee extension 2 |   |
| Knee extension 3 |   |
| Knee extension 4 |   |
| Knee extension 5 |   |

Pain test / 10 ________

Strength test / Biodex ISOKINETIC 90°/s
ROM peak torque
| Knee extension 1 |   |
| Knee extension 2 |   |
| Knee extension 3 |   |
| Knee extension 4 |   |
| Knee extension 5 |   |

Pain test / 10 ________
**Strength test / Biodex ISOKINETIC 120°/s**

ROM peak torque

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Knee Lever Length___________
Pain 1 test / 10 _______
Appendix C

Consent Form

I have agreed to participate in a study entitled “Perceived level of disability in individuals diagnosed with knee osteoarthritis”.
I understand that:

1) This is a research project being conducted through the School of Rehabilitation Therapy at Queen’s University and the Department of Surgery at Hotel Dieu Hospital. The principal investigators are Dr. Alice Aiken, Dr. Mark Harrison and Kamary Coriolano Da Silva PhD (candidate).

2) This study is being conducted to collect the perceived level of disability of obese individuals diagnosed with knee osteoarthritis and to associate their perceived level of disability with measures of physical and psychological function.

3) I am being asked to fill out several questionnaires, perform some simple functional tests that involve walking and sitting. It will take approximately 90 minutes of my time to complete the questionnaires and perform the functional tests.

4) I am being asked to wear a Biopeak Biofusion monitor when the functional tests are performed. This monitor allows for a broader range of high-quality physiological parameters to be measured, such as bioelectrical impedance analysis (BIA). BIA is measured when a small, safe electrical signal is passed through the body, carried by water and fluids. By using the impedance measurements it is possible to calculate the percentage of body fat, fat-free mass, hydration level, and other body composition values.

5) There are no anticipated benefits from my participation in this study, and there is a minor risk of fatigue but I can rest or stop testing if I become fatigued.

6) My medical charts will be reviewed by the researchers to look at the results of any diagnostic tests (eg. X-rays) and to determine any medical conditions I may have.

7) My testing and survey information will be kept strictly confidential, identifiable only by a code.

8) All surveys and testing information will be kept in a locked filing cabinet and will be available only to the principal investigators. Any data collected will be presented as group data only, so my individual responses will not be identifiable.

9) My participation in this study is voluntary. I may refuse to answer any question that I do not feel comfortable answering. I may withdraw from the study at any time without penalty and this will not affect my care in the orthopaedic clinic.

10) If I have any questions about my participation in this study, or would like to have my data removed from the study I may do so by contacting:
    a) the principal investigators, Kamary Coriolano Da Silva at (613) 533-6000 ext. 79386 or 5ldske@queensu.ca, or Dr. Alice Aiken at (613) 533-6710 or alice.aiken@queensu.ca, or
    b) the Department Head, Dr. John Rudan at (613) 549.6666 ext.3670, or
    c) If I have any questions regarding my rights as a research subjects, I may contact Dr. Albert Clark, Chair of Research Ethics Board at (613) 533-6081.

________________________________________  __________________________
Signature of Patient  Date
Appendix D
Letter of Information

You are invited to participate in a study entitled “Perceived level of disability in individuals diagnosed with knee osteoarthritis”. This is a research project being conducted through the Department of Surgery at Hotel Dieu Hospital and the School of Rehabilitation Therapy at Queen’s University. The principal investigators are Kamary Coriolano Da Silva PhD (candidate), Dr. Mark Harrison and Dr. Alice Aiken. This study will collect the perceived level of disability of participant’s diagnosed with knee OA and control participants using self-report questionnaires. On the same session, objective measures of physical and psychological function will also be collected.

In this study you will be asked to fill out several questionnaires, perform some simple functional tests that involve walking and sitting. It will take approximately 90 minutes of your time to complete the questionnaires and perform the functional tests. There are no direct benefits from your participation in this study. We might suggest ways to improve your quality of life, and increase your level of physical activity, in a safe, motivating, pleasant and accessible way. There is a minor risk of fatigue while you are performing the test; however the research assistant will allow you to rest as much as you like, and you may refuse to continue if you get too fatigued. You will be asked to wear a Biopeak Biofusion monitor while the functional tests are performed. This monitor will allow us to assess the effect of body weight on perceived levels of disability in individuals with knee OA. The monitor calculates the body fat mass and free-fat mass obtained with bioelectrical impedance analysis. Your medical chart will be reviewed by the researchers or their assistants to look at the results of any diagnostic tests (eg. X-rays) and to determine any medical conditions you may have. The information from your questionnaires and tests will be kept strictly confidential, identifiable only by a code. All test data and surveys will be kept in a locked filing cabinet and will be available only to the principle investigators and the research team.

Collaboration with the Institute National de la recherche scientifique (INRS) at the Energy Materials Telecommunications Research Center (EMT) from Université du Quebec in Montreal, will give the opportunity to develop a multimodal fitness indicator based on physiological signals harnessed non-invasively with Biopeak’s BioFusion. Any data collected will be presented as group data only, so your individual responses will not be identifiable. It should be noted that only numerical data will be accessed by the INRS-EMT team and participants will be only identified by a code. The numerical data will be safety kept in an encrypted file in a computer accessed only with a password.

Your participation in this study is voluntary. You may refuse to answer any questions that you do not feel comfortable answering. You may withdraw from the study at any time and this will not affect your care in the orthopaedic clinic. If you have any questions about your participation in this study, or would like to have your data removed from the study you may do so by contacting the principal investigators, Dr. Alice Aiken, at (613) 533-6710 or alice.aiken@queensu.ca, or Dr. Mark Harrison at (613) 549-6666 ext. 4537 or harissom@KGH.KARI.NET, Kamary Coriolano Da Silva at (613) 533-6000 ext. 79386 or 5ldskc@queensu.ca, or the department Head of the Department of Surgery, Dr. John Rudan at (613) 549.6666 ext.3670 or rudanj@KGH.KARI.NET. If you have any questions regarding your rights as a research participant, you may contact Dr. Albert Clark, Chair, and Research Ethics Board at (613) 533-6081.

If you agree to participate, please sign the attached consent form and submit it to the research assistant. Please keep this letter so you have all the appropriate contact information.

Thank you very much for taking the time to participate in this study.

Sincerely,

Kamary Coriolano
Appendix E

Calculation of peak oxygen uptake in upper body:

**FEMALES**

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<th>(L·min(^{-1})) 900g (63 watt)</th>
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</table>

Accuracy expressed as Standard error of the estimate (% VO_{max}) is 10.7 % for the women.

Divide the liter·min\(^{-1}\) value from the table by body weight to express the peak oxygen uptake in upper body in mL·kg\(^{-1}\)·min\(^{-1}\):

\[
\text{Peak oxygen uptake in mL·kg}^{-1}\cdot\text{min}^{-1} = (\text{L} \cdot \text{min}^{-1}) \cdot \frac{1000}{\text{BW}^{-1}}
\]
### MALES

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<tr>
<th>HR</th>
<th>300g (21 watt)</th>
<th>VO_{peak} 600g (42 watt)</th>
<th>(L·min⁻¹) 900g (63 watt)</th>
<th>1.2kg (84 watt)</th>
<th>1.5kg (105 watt)</th>
<th>1.8kg (126 watt)</th>
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</table>

Accuracy expressed as Standard error of the estimate (% VO_{peak}) is 11.8 % for the men.

Divide the liter value by body weight to express the peak oxygen uptake in upper body in mL·kg⁻¹·min⁻¹ (VO_{peak}):

Peak oxygen uptake in mL·kg⁻¹·min⁻¹ = L·min⁻¹ · 1000/ BW⁻¹
Appendix F

Description of recruitment

All participants were recruited from the orthopedic surgical case load of one participating orthopedic surgeon at Kingston General Hospital, Kingston, Ontario, Canada. Patients were identified as potential participants for the study by the surgeon during an initial consultation. Those who showed moderate to severe radiological knee OA using the Kellgren-Lawrence Scale were invited to participate in the study. After the consultation with a patient, the orthopedic surgeon talked to the researcher and informed him whether the patient would be a potential candidate for Total Knee Replacement (TKR) surgery and whether his radiological information indicated appropriateness for the study criteria. If the patient was appropriate, the orthopedic surgeon returned to the room with the researcher and introduced the researcher to the patient. The researcher subsequently described the study procedures and asked whether the patient would be willing to participate. If he/she agreed, an information letter was provided and informed consent was obtained.

This study population was a sample of convenience and 50 patients were invited to participate but only 31 were eligible to participate. Of the 19 participants, 12 could not participate because they were not eligible according to our exclusion criteria. The other 7 participants were from rural areas or from further locations outside of Kingston, therefore, transportation was an issue and these 7 individuals could not participate.

Inclusion Criteria:

1. Participants had to be diagnosed with knee OA according to the Kellgren-Lawrence radiological scale and those with OA severity of two or higher were invited to participate in the study.
   a. If any participant had radiological knee OA in both knees, the isokinetic muscle testing focused the side where the diagnosed knee OA showed higher level of severity or the one to be operated first.
**Exclusion Criteria:**

1- To able to tolerate moderate activity for 60 to 90 minutes.

2- To be free from severe comorbidities that would prevent them from participating in the study, such as unstable angina and/or heart disease, uncontrolled blood pressure (systolic pressure > 140 mmHg, diastolic pressure > 90 mmHg) and non-knee OA related mobility restrictions (neurological: stroke, Parkinson’s and etc. or musculoskeletal: muscle dystrophy, previous on the opposite knee, muscle injury and etc.).

3- Pain medication was not a criterion for exclusion: If any patients had to be under high dosage of any strong medication for pain, the information about the medication would be obtained. However, any other type of medication that caused decrease in balance or dizziness or limited participant functional capacity would be considered as a criterion for exclusion, if the medication could not be taken after tests.

---

**Participant Recruitment Chart**

- **50 Participants involved**
  - **31 were eligible**
    - **15 Health control subjects**
    - **15 Obese**
    - **16 Non-obese**
  - **12 were excluded due to other comorbidities**
  - **7 withdrawn not able to return due to transportation**
Groups’ description:

The obese and non-obese groups consisted of 31 individuals diagnosed with knee OA by the participating orthopedic surgeon. Of 31 individuals diagnosed with knee OA, 15 were considered obese (BMI ≥ 30 kg/m²) and 16 were non-obese. Specifically, of the 16 non-obese participants, 9 were overweight (BMI = 25–29.9 kg/m²) and 7 were healthy weight (BMI = 18.5–24.9 kg/m²). It was very difficult to recruit patients within a BMI category of 18.5-24.9 kg/m² during consultation with the support of only one orthopedic surgeon. Further information about non-obese group is found under Data Analysis, under the subtopic called: Manipulation checks and group composition analyses on chapter 3, 4 and 5.

For Chapter 5, all 15 health control subjects matched the obese OA and non-obese OA groups in age and gender. Therefore, no significant differences in age and gender were observed between healthy control subjects and OA groups. The control group was recruited from the local community through advertisements and the data from these individuals was used on chapter 5 only.
Appendix G

WOMAC OSTEOARTHRITIS INDEX

1. The following questions concern the amount of pain you are currently experiencing in your knees. For each situation, please enter the amount of pain you have experienced in the past 48 hours.

<table>
<thead>
<tr>
<th>A. Walking on a flat surface</th>
<th>None</th>
<th>mild</th>
<th>moderate</th>
<th>severe</th>
<th>extreme</th>
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</thead>
<tbody>
<tr>
<td>B. Going up or down stairs</td>
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<td>C. At night while in bed</td>
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<tr>
<td>D. Sitting or lying</td>
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<tr>
<td>E. Standing upright</td>
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</table>

2. Please describe the level of pain you have experienced in the past 48 hours for each one of your knees.

<table>
<thead>
<tr>
<th>A. Right knee</th>
<th>None</th>
<th>mild</th>
<th>moderate</th>
<th>severe</th>
<th>extreme</th>
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<tbody>
<tr>
<td>B. Left knee</td>
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</table>

3. How severe is your stiffness after first awakening in the morning?

None mild moderate severe extreme

4. How severe is your stiffness after sitting, lying, or resting later in the day?

None mild moderate severe extreme

5. 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 48 hours, in your knees. What degree of difficulty do you have with:

| 1. Descending (going down) stairs | None | mild | moderate | severe | extreme |
| 2. Ascending (going up) stairs    |      |      |          |        |         |
| 3. Rising from sitting           |      |      |          |        |         |
| 4. Standing                      |      |      |          |        |         |
| 5. Bending to floor              |      |      |          |        |         |
| 6. Walking on a flat surface     |      |      |          |        |         |
| 7. Getting in/out of car         |      |      |          |        |         |
| 8. Going shopping                |      |      |          |        |         |
| 9. Putting on socks/stockings    |      |      |          |        |         |
| 10. Rising from bed              |      |      |          |        |         |
| 11. Taking off socks/stockings   |      |      |          |        |         |
| 12. Lying in bed                 |      |      |          |        |         |
| 13. Getting in/out of bath       |      |      |          |        |         |
| 14. Sitting                      |      |      |          |        |         |
| 15. Getting on/off toilet        |      |      |          |        |         |
| 16. Heavy domestic duties        |      |      |          |        |         |
| 17. Light domestic duties        |      |      |          |        |         |
Beck's Depression Inventory

This depression inventory can be self-scored. The scoring scale is at the end of the questionnaire.

1. 0 I do not feel sad.
    1 I feel sad.
    2 I am sad all the time and I can't snap out of it.
    3 I am so sad and unhappy that I can't stand it.

2. 0 I am not particularly discouraged about the future.
    1 I feel discouraged about the future.
    2 I feel I have nothing to look forward to.
    3 I feel the future is hopeless and that things cannot improve.

3. 0 I do not feel like a failure.
    1 I feel I have failed more than the average person.
    2 As I look back on my life, all I can see is a lot of failures.
    3 I feel I am a complete failure as a person.

4. 0 I get as much satisfaction out of things as I used to.
    1 I don't enjoy things the way I used to.
    2 I don't get real satisfaction out of anything anymore.
    3 I am dissatisfied or bored with everything.

5. 0 I don't feel particularly guilty.
    1 I feel guilty a good part of the time.
    2 I feel quite guilty most of the time.
    3 I feel guilty all of the time.

6. 0 I don't feel I am being punished.
    1 I feel I may be punished.
    2 I expect to be punished.
    3 I feel I am being punished.

7. 0 I don't feel disappointed in myself.
    1 I am disappointed in myself.
    2 I am disgusted with myself.
    3 I hate myself.

8. 0 I don't feel I am any worse than anybody else.
    1 I am critical of myself for my weaknesses or mistakes.
    2 I blame myself all the time for my faults.
    3 I blame myself for everything bad that happens.

9. 0 I don't have any thoughts of killing myself.
    1 I have thoughts of killing myself, but I would not carry them out.
    2 I would like to kill myself.
    3 I would kill myself if I had the chance.

10. 0 I don't cry any more than usual.
     1 I cry more now than I used to.
     2 I cry all the time now.
     3 I used to be able to cry, but now I can't cry even though I want to.
11. I am no more irritated by things than I ever was.
0 I am slightly more irritated now than usual.
1 I am quite annoyed or irritated a good deal of the time.
2 I feel irritated all the time.

12. I have not lost interest in other people.
0 I am less interested in other people than I used to be.
1 I have lost most of my interest in other people.
2 I have lost all of my interest in other people.

13. I make decisions about as well as I ever could.
0 I put off making decisions more than I used to.
1 I have greater difficulty in making decisions more than I used to.
2 I can't make decisions at all anymore.

14. I don't feel that I look any worse than I used to.
0 I am worried that I am looking old or unattractive.
1 I feel there are permanent changes in my appearance that make me look unattractive.
2 I believe that I look ugly.

15. I can work about as well as before.
0 It takes an extra effort to get started at doing something.
1 I have to push myself very hard to do anything.
2 I can't do any work at all.

16. I can sleep as well as usual.
0 I don't sleep as well as I used to.
1 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
2 I wake up several hours earlier than I used to and cannot get back to sleep.

17. I don't get more tired than usual.
0 I get tired more easily than I used to.
1 I get tired from doing almost anything.
2 I am too tired to do anything.

18. My appetite is no worse than usual.
0 My appetite is not as good as it used to be.
1 My appetite is much worse now.
2 I have no appetite at all anymore.

19. I haven't lost much weight, if any, lately.
0 I have lost more than five pounds.
1 I have lost more than ten pounds.
2 I have lost more than fifteen pounds.
20. 0  I am no more worried about my health than usual.
        1  I am worried about physical problems like aches, pains, upset stomach, or constipation.
        2  I am very worried about physical problems and it's hard to think of much else.
        3  I am so worried about my physical problems that I cannot think of anything else.

21. 0  I have not noticed any recent change in my interest in sex.
        1  I am less interested in sex than I used to be.
        2  I have almost no interest in sex.
        3  I have lost interest in sex completely.
SF-36 QUESTIONNAIRE

Name: __________________________  Ref. Dr: __________________________  Date: ________

ID#: __________________________  Age: ________  Gender: M / F

Please answer the 36 questions of the Health Survey completely, honestly, and without interruptions.

GENERAL HEALTH:
In general, would you say your health is:
○ Excellent  ○ Very Good  ○ Good  ○ Fair  ○ Poor

Compared to one year ago, how would you rate your health in general now?
○ Much better now than one year ago
○ Somewhat better now than one year ago
○ About the same
○ Somewhat worse now than one year ago
○ Much worse than one year ago

LIMITATIONS OF ACTIVITIES:
The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.
○ Yes, Limited a lot  ○ Yes, Limited a Little  ○ No, Not Limited at all

Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf
○ Yes, Limited a Lot  ○ Yes, Limited a Little  ○ No, Not Limited at all

Lifting or carrying groceries
○ Yes, Limited a Lot  ○ Yes, Limited a Little  ○ No, Not Limited at all

Climbing several flights of stairs
○ Yes, Limited a Lot  ○ Yes, Limited a Little  ○ No, Not Limited at all

Climbing one flight of stairs
○ Yes, Limited a Lot  ○ Yes, Limited a Little  ○ No, Not Limited at all

Bending, kneeling, or stooping
○ Yes, Limited a Lot  ○ Yes, Limited a Little  ○ No, Not Limited at all

Walking more than a mile
○ Yes, Limited a Lot  ○ Yes, Limited a Little  ○ No, Not Limited at all

Walking several blocks
○ Yes, Limited a Lot  ○ Yes, Limited a Little  ○ No, Not Limited at all

Walking one block
○ Yes, Limited a Lot  ○ Yes, Limited a Little  ○ No, Not Limited at all
Bathing or dressing yourself
☐ Yes, Limited a Lot ☐ Yes, Limited a Little ☐ No, Not Limited at all

PHYSICAL HEALTH PROBLEMS:
During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

☐ Cut down the amount of time you spent on work or other activities
☐ No

☐ Accomplished less than you would like
☐ No

☐ Were limited in the kind of work or other activities
☐ No

☐ Had difficulty performing the work or other activities (for example, it took extra effort)
☐ No

EMOTIONAL HEALTH PROBLEMS:
During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

☐ Cut down the amount of time you spent on work or other activities
☐ No

☐ Accomplished less than you would like
☐ No

☐ Didn't do work or other activities as carefully as usual
☐ No

SOCIAL ACTIVITIES:
Emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?
☐ Not at all ☐ Slightly ☐ Moderately ☐ Severe ☐ Very Severe

PAIN:
How much bodily pain have you had during the past 4 weeks?
☐ None ☐ Very Mild ☐ Mild ☐ Moderate ☐ Severe ☐ Very Severe

During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?
☐ Not at all ☐ A little bit ☐ Moderately ☐ Quite a bit ☐ Extremely
ENERGY AND EMOTIONS:
These questions are about how you feel and how things have been with you during the last 4 weeks. For each question, please give the answer that comes closest to the way you have been feeling.

Did you feel full of pep?
☐ All of the time
☐ Most of the time
☐ A good Bit of the Time
☐ Some of the time
☐ A little bit of the time
☐ None of the Time

Have you been a very nervous person?
☐ All of the time
☐ Most of the time
☐ A good Bit of the Time
☐ Some of the time
☐ A little bit of the time
☐ None of the Time

Have you felt so down in the dumps that nothing could cheer you up?
☐ All of the time
☐ Most of the time
☐ A good Bit of the Time
☐ Some of the time
☐ A little bit of the time
☐ None of the Time

Have you felt calm and peaceful?
☐ All of the time
☐ Most of the time
☐ A good Bit of the Time
☐ Some of the time
☐ A little bit of the time
☐ None of the Time

Did you have a lot of energy?
☐ All of the time
☐ Most of the time
☐ A good Bit of the Time
☐ Some of the time
☐ A little bit of the time
☐ None of the Time
Have you felt downhearted and blue?
- All of the time
- Most of the time
- A good bit of the time
- Some of the time
- A little bit of the time
- None of the Time

Did you feel worn out?
- All of the time
- Most of the time
- A good bit of the time
- Some of the time
- A little bit of the time
- None of the Time

Have you been a happy person?
- All of the time
- Most of the time
- A good bit of the time
- Some of the time
- A little bit of the time
- None of the Time

Did you feel tired?
- All of the time
- Most of the time
- A good bit of the time
- Some of the time
- A little bit of the time
- None of the Time

SOCIAL ACTIVITIES:
During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?
- All of the time
- Most of the time
- Some of the time
- A little bit of the time
- None of the Time
GENERAL HEALTH:
How true or false is each of the following statements for you?

I seem to get sick a little easier than other people
☐ Definitely true ☐ Mostly true ☐ Don't know ☐ Mostly false ☐ Definitely false

I am as healthy as anybody I know
☐ Definitely true ☐ Mostly true ☐ Don't know ☐ Mostly false ☐ Definitely false

I expect my health to get worse
☐ Definitely true ☐ Mostly true ☐ Don't know ☐ Mostly false ☐ Definitely false

My health is excellent
☐ Definitely true ☐ Mostly true ☐ Don't know ☐ Mostly false ☐ Definitely false