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Physical activity and sedentary behaviour patterns in patients with knee osteoarthritis

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PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR PATTERNS IN PATIENTS WITH KNEE OSTEOARTHRITIS

Yusuf Suleiman Kaoje

A dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand, in fulfilment of the requirements for the degree of Master of Science in Medicine

Johannesburg, South Africa, 2017

DECLARATION

I, Yusuf Suleiman Kaoje, declare that the work contained in this dissertation is my own, except where others have helped as indicated in the acknowledgements and the reference list. This dissertation is being submitted for the degree of Master of Science in Medicine in the Faculty of Health Sciences at the University of the Witwatersrand,
Johannesburg, South Africa. It has not been submitted before for any degree or examination at any University. I certify that all the experimental procedures used in this dissertation were approved by the Human Ethics Research Committee of the University of the Witwatersrand (protocol clearance number: M 150323).

.....

Yusuf Suleiman Kaoje

Signed on the 30th day of November 2017.

DEDICATION

To Professor Bello Bala Shehu My Father and Mentor without whom I would not be where I am today. You saw a potential which no one saw and nourished it. Thank you for believing in me.

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CONFERENCE PRESENTATION

I was privileged to present a poster at the 15th International Society of Behavioural Nutrition and Physical Activity (ISBNPA) meeting in Cape Town 8-11 of June 2016, and at the 44th Congress of the Physiology Society of Southern Africa (PSSA), Cape Town 28-31 of August 2016, using data from this study.

Title of presentation: Suleiman Y.K., McVeigh J.A., Meiring R.M. Sedentary behaviour patterns in patients with knee osteoarthritis

Manuscript in preparation:

Suleiman Y, Van der Jagt D, McVeigh JA and Meiring RM. Patterns of physical activity and sedentary behaviour in patients with knee osteoarthritis waiting for total knee replacement. Proposed journal: *Journal of physical activity and ageing.*

I was also involved in data collection, analysis and draft editing of the following paper which is under review at *Knee Surgery, Sports Traumatology, Arthroscopy.*

Frimpong E, McVeigh JA, van der Jagt D, Mokete L, Kaoje Y, Tikly M and Meiring RM. Changes in volume and patterns of objectively measured physical activity and sedentary behaviour following total knee arthroplasty: A longitudinal study.

ACKNOWLEDGEMENTS

Firstly I would like to extend my sincere gratitude to my supervisors Dr Rebecca Meiring and Dr Jo McVeigh for their scientific input, patience, motivation, immense knowledge and write up process of this dissertation. Thank you, I would not get better teachers.

I would also like to thank Prof Mohammed Tikly and Prof Dick Van Der Jagt for their input in analysis of this dissertation and also a very special thanks to Emmanuel Frimpong who guided me through the whole process of my dissertation.

My sincere thanks also goes to Dr Lipalo Mokete, Dr Jurek Pietrzak and the entire Arthroplasty team especially Mrs. Mathabe for their resilient support in the recruitment process of the participants.

I am truly grateful to David Goble for helping through editing my work and also to my lab mates for their support.

My special thanks to a very good friend Dr Vernice Peterson, not only did she put me through research writing but her moral support was exceptional.

My sincere appreciation to the head of school and the entire members of the school of physiology, thank you for a wonderful experience.

Last but not the least I would like to say a very big thank you my Family and Friends who have been with me with their prayers and love from the beginning of this wonderful journey of my life experience.

ABSTRACT

Objective: Physical activity (PA) is recommended in the management of osteoarthritis (OA) to reduce pain and improve function. Total volumes of PA and sedentary behaviour (SB) have been described in people with knee OA, but detailed information about the patterns of accumulation of PA and SB in knee OA populations is lacking. The purpose of this study was to objectively assess the patterns of accumulation of PA and SB and to explore associations with subjectively measured functional outcomes and quality of life in patients with knee OA.

Methods: End-stage knee OA patients (n = 87, 65 ± 8.8 (mean ± SD) years, body mass index 34.4 ± 7.8 kg/m^2) with Kellgren-Lawrence-defined grade 3-4 radiographic OA, wore an Actigraph and an activPAL accelerometer for 24 hours a day for 7 consecutive days. Total volumes of SB, light physical activity (LPA), moderate to vigorous physical activity (MVPA), and different bouts of SB, LPA, and MVPA were assessed. Self-report questionnaires were used to assess patient-experienced pain, function, quality of life and activities of daily living were the Western Ontario and McMaster Universities (WOMAC) osteoarthritis index and the Knee Injury Osteoarthritis Outcome Score (KOOS).

Results: Of the 87 knee OA patients only 76 and 65 had complete Actigraph and activPAL data respectively. The participants had a mean (SD) age of 65.0 (8.8) years, were mostly women and most were classified as being obese with an average BMI of 34.4 (7.8) kg/m^2. The Actigraph mean (95% CI) of awake wear time was 15.6 (15.1-16) hours/day, SB 10.9 (10.5-11.4) hours/day, LPA 4.5 (4.1-5) hours/day and MVPA 8.2 (3.3-13) min/day. Approximately 7% of patients met the current recommended PA guidelines. The activPAL mean (95% CI) of sitting time, standing time, stepping time and number of steps were 9.3 (8.5 – 10.1) hours per day, 5.0 (4.4 – 5.6) hour per day, 76.5 (66.6 – 86.3) minutes per day and 2489 (2130 – 2848) minutes per day respectively. There were variations in the hourly patterns of movement behaviours. Participants were significantly less sedentary between 6 am and 9 am compared to the grand mean of sedentary time per hour over the day ($p<0.01$) and were significantly more sedentary per hour from 3 pm to 7 pm ($p<0.05$). Significant correlations were found between WOMAC pain scores and Actigraph measured SB (r=0.277, p=0.031), LPA (r=-0.240, p=0.043), MVPA (r=-0.242. p=0.042), number of steps (r=-0.282, p=0.020), number of breaks in bouts of SB greater than 20 minutes (r=-0.292,

p=0.016), average duration of breaks in SB (r=-0.277, p=0.024), average duration of MVPA bouts (r=-0.326, p=0.012). Significant correlations were also found between WOMAC activity of daily living scores and Actigraph measured LPA (r=-0.206, p=0.048), MVPA (r=-0.246, p=0.029), number of steps (r=-0.286, p=0.010) and average duration of MVPA bouts (r=-0.383, p=0.002). Significant correlations were found between WOMAC pain scores and activPAL sitting time (r=0.029, p=0.02), and stepping time (r=-0.029, p=0.01), between self-reported WOMAC activity of daily living score and stepping time (r=-0.309, p=0.02), between KOOS activity of daily living score and stepping time (r=-0.276, p=0.004), and between KOOS quality of life score and stepping time (r=-0.263, p=0.008).

Conclusion: This study describes novel detail of the patterns of activity and sedentary behaviour in patients with knee OA. The use of two accelerometers gives a detailed account of daily activity and the variation throughout the day, highlighting when interventions to improve activity might be most effective. Therefore, interventions should target the long bouts of inactivity in this population. Since even healthy populations of older adults struggle to meet current recommended PA guidelines, it may be important to shift attention from meeting recommendations of MVPA to creating feasible suggestions of doing more light activity and breaking more sedentary time in knee OA patients.

LIST OF ABBREVIATIONS

ACSM – American College of Sports Medicine

CDC – Centre for Disease Control and Prevention

DHHS – Department of Health and Human Services

EE - Energy Expenditure

LPA – Light Physical Activity

METs – Metabolic Equivalents

MPA – Moderate Physical Activity

VPA - Vigorous Physical Activity

MVPA - Moderate and Vigorous activity

NSAID - Non-Steroidal Anti-inflammatory Drug

OA - Osteoarthritis

PA – Physical Activity

SB - Sedentary behaviour

SC - Step count

WT - Wear time

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CHAPTER 1: INTRODUCTION

It has been estimated that by the year 2050 about 130 million people will be affected by osteoarthritis (OA) worldwide, with about 40 million people severely disabled by the disease (Brolan et al., 2013).
Major risk factors for this disease are obesity, older age, female gender and trauma to the joint (Dillon et al., 2006). The leading cause of disability in older adults is knee OA (Helmick et al., 2008; Yelin, 2003; Felson et al., 2000), which limits the ability to perform activities of daily living due to the presence of knee pain (American Geriatrics Society Panel on Exercise and Osteoarthritis, 2001).

Participation in physical activity (PA) however, delays loss of muscle strength, physical function and reduces the symptoms of knee OA (Chmelo et al., 2013), confirming the importance of taking part in sufficient physical activity by people with knee OA. Physical activity was introduced by the American Geriatrics Society, and the American College of Rheumatology as a preventative measure of knee OA and in the management of patients with knee OA (Fontaine et al., 2004; Chang et al., 2003; American Geriatrics Society Panel on Exercise and Osteoarthritis, 2001). Older adults, including those with knee OA, should perform 150 minutes of physical activity of moderate to vigorous intensity per week (Garber et al., 2011), which may be difficult to achieve in a population with a mobility disorder. Some studies that measured moderate to vigorous physical activity (MVPA) in knee osteoarthritis patients reported that between 3 - 40% of patients, with varying degrees of disease severity, meet the recommended guidelines (Lee et al., 2013; Dunlop et al., 2011a; S. M. Tonelli et al., 2011; Hootman et al., 2003). Studies have shown that even healthy older adults do not meet the recommended guidelines of 150 minutes per week of MVPA (Jefferis et al., 2014; Tucker et al., 2011). Compared to the general population, this level of physical activity is considerably lower as between 50-60% of young healthy adults meeting the recommended PA guidelines (McVeigh et al., 2016) and globally 31% of adults are physically *inactive* (WHO, 2017).

Another important activity behaviour that can be measured is sedentary behaviour (SB). Sedentary behaviour consists of activities that require energy expenditures similar to those

of resting levels i.e. between 1.0 – 1.5 metabolic equivalents (METs) (Pate et al., 1995). Knee OA patients who are more sedentary have a poorer functional capacity compared to those who are less sedentary (Semanik et al., 2015).

The pain and early morning stiffness (which lasts about 30 mins) that these patients usually present with is what makes them seek treatment, because it affects their daily functional performance, which makes knee OA patients less active and very sedentary. However, it should be noted that most measurements of activity in knee OA patients have been done using self-report. Studies that have measured PA and SB in knee OA patients have generally only measured the total volume of activity behaviours in knee OA patients but how the total volume is accumulated (i.e. the patterns of activity behaviours) have not been explored extensively. The limitation of only measuring the average amount of time spent in different intensities of activity per day is that the detailed descriptions of activity might not be captured. For example, the times of the day of when and how activity patterns are accumulated might be missed.

Therefore, a detailed study measuring these activity behaviour patterns in a population with a mobility disorder such as knee OA is critical in understanding how people with knee OA move throughout the course of a typical day and week. Knowing such information gives effective reasoning for attempting to encourage people with knee OA to move more and sit less at times of the day that may be more pain free. Targeted and informed interventions may then be developed specifically for increasing PA and decreasing SB in this population.

1.1. Aims, Objectives and hypotheses

The aims of this study were to:

1. Describe the levels and patterns of physical activity and sedentary behaviour in patients with knee osteoarthritis.
2. Determine if the levels and patterns of physical activity and sedentary behaviour are related to differences in subjectively measured functional outcomes and quality of life in patients with knee osteoarthritis.

The objectives of the study were:

1. To objectively measure the levels of total time spent in various intensities of physical activity and in sedentary behaviour in patients with knee osteoarthritis through the use of accelerometry.

2. To determine the patterns of physical activity and sedentary behaviour in patients with knee osteoarthritis through the use of accelerometry.

3. To determine whether the patterns of objectively measured physical activity and sedentary behaviour in patients with knee osteoarthritis fluctuate over the course of a day and a week.

4. To examine the association between objectively measured physical activity and sedentary behaviour with self-reported knee osteoarthritis functional outcomes and quality of life.

CHAPTER 2: LITERATURE REVIEW

2.1. Osteoarthritis

Osteoarthritis (OA) is an articular cartilage degenerative disorder associated with hypertrophic changes of the bone (Sinusas, 2012). In addition to cartilage degeneration, OA also affects the capsule, tendons, periarticular bones, ligaments and muscles of the affected joint (Goldring and Goldring, 2007). Osteoarthritis is the most common form of arthritis and a major cause of pain and disability in older adults (Lubar et al., 2010). Various biochemical, biomechanical, inflammatory and immunologic factors are responsible for the functional and structural changes that occur in OA (Lajeunesse and Reboul, 2003) yet there is no known cause of OA. The most commonly affected joint in OA is the knee, with 41% of limb arthritis occurring in the knee compared to 30% and 19% in the hands and hips, respectively (Wood et al., 2013). According to the American College of Rheumatology (ACR) criteria, classification and diagnosis of knee OA is either by clinical and laboratory criteria, clinical and radiographic criteria, or clinical criteria only (

Table **0.1**) (Altman et al., 1986). Radiographic knee OA changes are observed in more than one third of adults 60 years and above, with only about 32% of the patients with radiographic knee OA presenting with pain and stiffness (Dillon et al., 2006). The low percentage of people being symptomatic suggests that most patients (about two thirds) with radiographic knee OA do not know they have OA and usually present at the clinic when the disease is at end stage.

The risk factors for knee OA include older age, occupational activities involving stooping, kneeling or crouching, previous knee trauma, female gender, genetic predisposition and mechanical factors such as malalignment or abnormal joint shape (Loeser et al., 2012; Blagojevic et al., 2010). Furthermore other predictors of reduced functionality in elderly knee OA patients include being overweight; smoking tobacco and having symptoms of depression (Mehrotra et al., 2003; Penninx et al., 2002).

Table 0.1 Criteria for the classification of idiopathic OA (Altman et al., 1986)

Clinical and laboratory	Clinical and radiographic	Clinical
Knee pain + ***at least 5 of 9 below:***	**Knee pain +** ***at least 1 of 3 below:***	**Knee pain +** ***at least 3 of 6 below:***
Age > 50 years	Age > 50 years	Age > 50 years
Stiffness< 30 minutes	Stiffness< 30 minutes	Stiffness< 30 minutes
Crepitus	Crepitus + Osteophytes	Crepitus
Bony tenderness		Bony tenderness
Bony enlargement		Bony enlargement
No palpable warmth		No palpable warmth
ESR < 40 mm/hr.		
RF < 1:40		
SF OA		

ESR= erythrocyte sedimentation rate (Westergren); RF = rheumatoid factor; SF OA = synovial fluid signs of OA (clear viscous, or white blood cell count < 2,000/mm^3).

In highlighting the major effects of obesity on knee OA risk, Losina et al (2011) generated a mathematical model of knee OA and obesity in order to estimate quality adjusted life year losses due to obesity and to determine the health benefits to knee OA if obesity prevalence was reduced to levels observed a decade ago (Losina et al., 2011). The model predicted that approximately six million people with symptomatic knee OA between the ages of 50-84 years collectively (obese and non-obese) would lose about 15 million quality adjusted life years. When considering only the 2.8 million non-obese persons with symptomatic knee OA, an estimated 5.2 million quality-adjusted life years would be lost, while almost double that would be lost by the obese patients with knee OA. If an individual (specifically an individual of five feet seven inches) reduced their BMI by 0.6 units (which was equivalent to a 1.7 kg reduction in body mass in that individual), 111,206 total knee replacements would be averted. Body mass index changes would increase life expectancy by 6,318,030

years and a quality of life improvement by 7,812,120 quality-adjusted life-years (Losina et al., 2011). The study concluded that if the prevalence of obesity was not on the increase, the incidence of knee OA would have been lower and more quality adjusted life years would be saved. The population most affected by these lost life years was projected to be black and Hispanic women (Losina et al., 2011). South African women have the highest rate of obesity among adults in sub-Saharan Africa with a value of 42%, while the combined rate of both overweight and obesity is 69.3%. South African men showed a 39% overall prevalence rate, with only a 14% obesity prevalence (Ng et al., 2014). Because being overweight or obese is such a big risk factor for knee OA and because the population of older adults is increasing (increased life expectancies), one might expect that knee OA will become an increasingly burdensome condition in South Africa.

2.2. Diagnosis of osteoarthritis

Joint pain is the most common symptom, followed by early morning stiffness. Diagnosis of OA is usually clinically based, and physicians reach diagnosis by taking history and with physical examination (Ickinger and Tikly, 2011) (Table 2.1).

2.3. Treatment of osteoarthritis

The key signs and symptoms of knee OA include pain, which is worsened with activity, morning joint stiffness lasting about 30 minutes (Sinusas, 2012), swelling, periarticular muscle atrophy, crepitus, joint line tenderness and joint instability (Ickinger and Tikly, 2011). Pain is the main reason patients seek medical attention as it is responsible for the decrease in functional performance and immobility experienced by patients with knee OA (Cubukcu et al., 2012). Treatment and/or management of OA is generally classified into four categories namely pharmacological, non-pharmacological, alternative and surgical (Sinusas, 2012). The goal of all knee OA treatments is the management of pain. However, total joint replacement surgery is the most effective intervention used if the other treatment methods have failed (Jordan et al., 2003). Indications of total joint replacement include

severe pain which is unresponsive to treatment, as well as radiographic evidence showing a reduction of joint space (Mancuso et al., 1996). Knee OA is a degenerative musculoskeletal disorder and there is no known cure, most patients at end stage eventually undergo a joint replacement (Manen et al., 2012).

Pharmacological treatment involves the use of drugs to alleviate pain and inflammation. Pain relief is important in the treatment of knee OA but not all patients require drug therapy. Those patients who do require drug therapy, may not need it all the time as they are able to cope on a functional basis (Sinusas, 2012). Pharmacological treatments include non-specific cyclooxygenase inhibitors (Vaishya et al., 2016), selective COX-2 inhibitors (Celecoxib, Rofecoxib, and Valdecoxib) (Brunton et al., 2005), opiates (Morphine, Codeine) (Vaishya et al., 2016), non-opioid oral analgesics (acetaminophen), nutraceuticals (Glucosamine) (Vaishya et al., 2016), antidepressants like amitriptyline, fluoxetine 2 (Brunton et al., 2005) and long-acting corticosteroid intra-articular injection (Jordan et al., 2003). All the above forms of treatment are targeted at relieving pain and reducing inflammation to improve daily functional performance and mobility.

Non-pharmacological management of knee OA usually involves encouraging weight loss in obese and overweight patients (Christensen et al., 2007), advising bracing and splinting in patients (Manek and Lane, 2000) and participation in regular exercise. The benefits of exercise on knee function in OA have been well documented; not only because of the weight loss associated with exercise (Garver et al., 2014), but also for the improvement in muscle function that occurs with participation in exercise programs (Oliveira et al., 2012). Saw and colleagues (2016) performed a randomised controlled trial at two public hospitals in South Africa. Two groups, an intervention (n=35) and a control (n=39) group, were formed from 74 participants on a waiting list for knee replacement surgery. The study showed that two hours of exercise every week from baseline until six months after knee surgery, had a moderate to large effect size on pain severity in the intervention group compared to the control group at six weeks and six months post-surgery [week 6: $p < 0.01$,

ES = 1.2, 95 % CI (0.70,1.69), week 12: p = 0.04, ES = 0.68, 95 % CI (0.20,1.14), month 6: p < 0.01, ES = 0.98, 95 % CI (0.49,1.45)]. There was also a reported moderate to large effect size on the reduction of pain that interfered with function at six weeks, 12 weeks and six months post-surgery (Saw et al., 2016). The latter study specifically demonstrated the post-surgical benefits of exercise on knee pain. However, a meta-analysis carried out by Fransen and McConnell (2008), where 3616 participants with knee OA were examined pre-surgically, showed that exercise was useful for the management of pain and improved physical function (Fransen and McConnell, 2008). Another study that focused on improving strength in the quadriceps muscles with an exercise regimen that lasted eight weeks, found an associated improvement in pain, function and stiffness in a group of knee OA patients (Oliveira et al., 2012). The aforementioned studies indicate that knee OA patients have benefited from structured exercise by reducing their pain experienced (Nejati et al., 2015; Fransen and McConnell, 2008). Similar to structured exercise studies benefitting knee OA, studies have also reported that better activity behaviours, such as daily activity at work or going shopping, or even how much time is spent watching television, also aid in reducing pain, and improving function in knee OA patients (Geneen et al., 2017; Song et al., 2017; Dunlop et al., 2014) . Better activity behaviours, like increasing levels of habitual activity, may benefit knee OA patients by enhancing weight loss and improving muscle strength around the knee joint.

Studies that have investigated activity behaviours in knee OA patients are highlighted in Table 0. and will be discussed in detail in section 2.7. The value of investigating activity behaviours in patients with mobility disorders, such as knee OA, lies in the promotion of a lifestyle change rather than the implementation of brief interventions, which may be effective for the duration of the intervention but do not change activity behaviours in the long-run. To change one's lifestyle, accurate and detailed assessment of daily activity behaviours needs to be made, to understand the variation in activity and the optimal times during the day for the possible promotion of beneficial activity behaviours. In addition, the relationship between knee function and activity behaviour patterns (which are considered a

less structured form of exercise like walking or climbing stairs) needs to be investigated in knee OA patients because there are so few studies that have looked at this relationship.

Alternative treatment includes acupuncture (Manheimer et al 2007), use of supplements such as chondroitin (Reichenbach et al 2008) and glucosamine (Clegg et al 2006), and treatments like spa therapy and mineral baths.

2.4. Activity behaviours

2.4.1. Habitual physical activity

Physical activity (PA) is "any bodily movement produced by skeletal muscle that results in caloric expenditure" (Control et al., 2008; Caspersen et al., 1985). On the other hand, exercise is a form of PA that is deliberate and designed to be repetitive and decisive (Caspersen et al., 1985). Resting energy expenditure (3.5 ml O_2 kg/min) is regarded as one metabolic equivalent (MET). As oxygen consumption increases with increasing intensities of PA, quantifying PA in multiples of resting metabolic equivalents (one MET) has become standard (e.g. any activity that requires two times the oxygen consumption of rest would be characterised as two METs) (Welk, 2002). Habitual physical activities include day to day activity behaviours that require energy expenditure above that of rest. These activities can vary in intensity with activities ranging from light - e.g. gardening (3 METs), to moderate to vigorous - e.g. activities involving running at about 5km/h (4.5 METs), or dancing (8.5 METs) (Ainsworth et al., 2000). The US Department of Health and Human Services (DHHS) recommends that older adults including those with arthritis should perform PA of 150 min/week or more of moderate to vigorous intensity (Hootman, 2009).

Recommendations based on intensity (measured in metabolic equivalents METS) made by the US Centres for Disease Control and Prevention (CDC) and American College of Sport Medicine (ACSM) classify PA as light (LPA; <3 METS), moderate (MPA; 3-6 METS) and vigorous (VPA; >6 METS). Older adults should also perform at least 30 minutes per day of

moderate intensity PA for at least 5 days per week (Control et al., 2008; Pollock et al., 1998).

2.4.2. Sedentary behaviour

Recently there has been prolific interest in the independent role that sedentary behaviour may play in deleterious health outcomes. Any activity that requires energy expenditure at a level of 1.0-1.5 metabolic equivalent units (METs) which includes activities like sitting, lying down, and television viewing (while sitting or lying down not while walking or running on the spot), during the awake hours of the day, is classified as SB (Pate et al, 2008). It has been shown that a higher sitting time is associated with an increased risk of mortality in healthy elderly women (Ekelund et al., 2016; Pavey et al., 2015).

2.5. Measuring physical activity and sedentary behaviour

2.5.1. The subjective measurement of physical activity and sedentary behaviour

Historically, PA has been measured subjectively in the elderly using the international physical activity questionnaire (IPAQ), global physical activity questionnaire (GPAQ) or the University of California Los Angeles activity index (UCLA). The IPAQ is available in two versions: the 9-item short form (IPAQ-SF), which measures activity in four intensity levels - vigorous, moderate, walking and sitting; and the 31-item long form (IPAQ-LF). The GPAQ was created by the World Health Organization (WHO) in 2002 and is composed of 19 questions where it measures PA in different domains which are organized leisure time physical activity (LTPA), work, transport and recreation. In each domain, the frequency and duration of activity are measured (Bull et al., 2009). Both the GPAQ and the IPAQ are suitable and acceptable tools for measuring physical activity (Bull et al., 2009). The UCLA on the other hand is a 10-point investigator-rated scale (1-10 with 1 indicating wholly inactive and 10 being regularly participates in contact sports) and is a convenient tool in assessing patient's activity levels. The UCLA has been validated and found to be reliable in assessing knee OA patients activity levels (Saleh et al., 2005). The advantages of self-reported measurement of PA is that it is a cost effective, time friendly, offer a wide

range of data (Prince et al., 2008) and are generally acceptable (Dishman et al., 2001). Based on evidence showing the relationship between activity data collected using the above questionnaires and outcomes such as mortality and risk of NCDs, researchers developed the 150 min/wk. of MVPA guidelines for the maintenance of cardiometabolic health (WHO 2011. However, studies have shown self-report data to be subjective, and vulnerable to recall bias (Liu et al., 2016; Schuna et al., 2013; Hertogh et al., 2008). Currently, the most reliable and objective way of measuring PA is through the use of accelerometers (Feito et al., 2012).

2.5.2. The objective measurement of physical activity and sedentary behaviour

Movement behaviours such as PA and SB can be measured using accelerometers (Welk, 2002). Accelerometers are small and portable devices that measure accelerations of body movement as counts per unit time (Alhassan et al., 2012). Measuring PA (using accelerometers) in a free-living environment or in a clinical setting is widely accepted. A seismic mass suspended by two beams are elements that make up the accelerometers (Scheeper et al., 1996). Deposited on top of the beams is a layer of piezoelectric material which is provided with two electrodes (Scheeper et al., 1996). The piezoelectric material becomes sensitive when responding to vertical and horizontal vibrations depending on the configuration of the electrodes on the two beams (Scheeper et al., 1996). The vibrations detected are converted to counts and the data are stored until they can be downloaded and analysed using established criteria. The use of accelerometers in different populations should follow best practice guidelines which advise on the type of monitor that should be used, the definition of wear days, the determination of epoch length and also the determination of monitor placement (Ward et al., 2005). To estimate habitual PA in adults, between three to five days of accelerometer monitoring is required (Trost et al., 2005). Because of the differences in weekend and weekday activities usually observed, monitoring for seven days is standard (Trost et al., 2005). The best position an accelerometer is mounted is on the hip or the lower back (Trost et al., 2005).

The measurement of PA by self-report tends to overestimate levels of PA (Conway et al., 2002; Irwin et al., 2001). Liu and colleagues used cross sectional data from the 2003-2006 National Health and Nutritional Examination Survey (NHANES) to compare self-report and accelerometer (AM-7164) measurement of PA in adults (45 years old and above), and discovered that self-report measurement of moderate to vigorous physical activity (MVPA) was 7 mins higher than that measured by accelerometer (Liu et al., 2016). The authors concluded that there was an over estimation of MVPA in participants with higher levels of education (Liu et al., 2016). A secondary analysis of participants from National Health and Nutrition Examination Survey (NHANES) carried out by Schuna et al (2013), measured PA subjectively and objectively and also discovered that activity levels were higher with self-report compared with accelerometry (Schuna et al., 2013). Lee and colleagues (2011) reviewed 23 studies that validated the IPAQ-SF against an objective PA device. Their results showed that correlations between self-report PA and objective methods were low and variable and concluded that objective measures of activity are more accurate and reliable than subjective measures (Lee et al., 2011). However, they are very expensive and their hardware, software and individual programming require expertise (Dishman et al 1994).

2.6. Types of accelerometers

The devices chosen for the current project were the activPAL and the ActiGraph. The activPAL has an inbuilt inclinometer which makes it more accurate in detecting postural changes from sitting to standing (Steeves 2015). It is also fitted with an accelerometer so that the time spent in varying intensities of activity can be calculated from the raw data based on previously developed cutpoints (Freedson 1998, Matthews 2008).

The ActiGraph is the most commonly used accelerometer and has customized software however the raw data can be extracted. This raw data can then be processed using publicly available and validated algorithms for the determination of a multitude of activity and sedentary behaviour variables (McVeigh et al., 2016).

Table 2.2 Different types of accelerometers

Measure	Location	Data Recorded	Output
Accelerometers			
Activpal	Thigh	Time spent in sedentary behaviour, standing and walking, Count of sit to stand transition, Total number of step for a given period	Energy expenditure per behaviour and time spent in each behaviours. The in-built inclinometer and its location of wear makes this device accurate in recording postural transitions. Raw data can be extracted.
Tritrac	Hip	Composite movement score (vector magnitude)	Energy expenditure per minute of movement, Estimate of resting metabolic rate
Tracmor	Lower back	Activity count per minute	Total energy expenditure, PA energy expenditure, PA levels, Activity energy expenditure per unit mass
Actigraph GT3X	Waist/Hip	Activity count (Amplitude and frequency) of acceleration over each sampling period	Activity intensity category, Time spent in sedentary, low, moderate, and intense activity. Algorithms have been specifically developed for this device which makes it the most commonly used device in studies of physical activity and sedentary behaviour in humans. Customised software but raw data can be extracted.
Actical	Waist/Hip	Activity counts, omnidirectional	Time spent in varying intensities of activity from applying count thresholds. Only accurate in one plane i.e. not tri-axial.

2.6.1. Actigraph GT3X+

In 2009, Actigraph produced the GT3X+ (ActiGraph, LLC, Fort Walton Beach, FL), which has an ADXL335 accelerometer (analog Devices, Norwood MA). The GT3X+ is a triaxial capacitive MEMS sensor with full scale range of ±3g. The GT3X+ is a lightweight (19g) and small (4.6cm by 3.3cm by 1.5cm) activity monitor which provides the following PA data; activity intensity, frequency of activity, duration of activity as well as energy expenditure (McMinn et al., 2013). Table 2.2 shows that the Actigraph can be worn on an elastic belt on the hip or waist. The Actigraph counts are converted into time spent in a certain intensity of activity based on published thresholds (Freedson et al., 1998). Counts per minute of an activity can be classified into sedentary behaviour (less than 100 counts per minute), light PA (less than 1951 counts per minute) and MVPA (1952 – 5724 counts per minute) (Freedson et al., 1998).

2.6.2. The activPAL

The activPAL (Physical Activity Technologies, Glasgow, Scotland) is a small, single unit activity monitor which can record posture and activity and is generally worn over a seven-day period (Davies et al., 2012). The activPAL accelerometer, which is worn on the mid-thigh (Table 2.2), fastened and secured by a non-allergenic adhesive tape, uses inclinometer and accelerometer derived information about thigh position to estimate time spent in different body positions in lying, sitting and standing and stepping (Kozey-Keadle et al., 2011). Data are collected in 15 sec epochs. The activPAL was also designed specifically to measure free living activity (Kozey-Keadle et al., 2011). Laboratory studies using the activPAL to obtain an estimate of time in different postures, sit-stand transitions (Grant et al., 2006), step counts (Maddocks et al., 2010; Ryan et al., 2006) and static and dynamic behaviour (Godfrey et al., 2007), have confirmed that the activPAL is more accurate and exact in calculating total sedentary time than is the GT3X+ (Kozey-Keadle et al., 2011).

2.7. Physical activity, sedentary behaviour, quality of life and functional outcomes in patients with knee OA

In knee OA patients, physical function is often used as a surrogate for activity during the day. Table 0.3 summarises studies that have used objective measures of PA and SB patients with knee OA. Two of these studies compared knee OA patients to a control group and found that PA is lower in knee OA patients (Verlaan et al., 2015; Holsgaard-Larsen and Roos, 2012). Verlaan et al (2015) aimed to assess the four components of PA (FITT - frequency, intensity, time, type) using a tri-axial accelerometer to examine 30 knee OA patients and 30 age matched controls. The study reported that the knee OA group was significantly less active than the control group in frequency of walking bouts, step counts and sit to stand transitions (Verlaan et al., 2015). Another study compared PA between 25 knee OA and 15 healthy controls using SenseWearTM Pro2 Arm-band (Body Media Inc., Pittsburgh, PA, USA) that was worn for five consecutive days including two weekend days and reported a lower step counts in knee OA patients compared to the healthy control group (Holsgaard-Larsen and Roos, 2012). Two studies highlighted that knee OA patients do not meet the current recommended PA guidelines. Farr et al (2008) found that their knee OA patients achieved only 24 minutes of MVPA per day (Farr et al., 2008), while Chmelo and colleagues reported their patients only taking part in 10 minutes of MVPA per day. In addition to low levels of PA (Chmelo et al., 2013), a few studies have reported that knee OA patients spend as much as two-thirds of their day (Lee et al., 2015; Semanik et al., 2015) in sedentary behaviour. There is however a paucity of literature on the objective measurement of SB in patients with knee OA. Also, no study in South Africa has looked at PA and SB patterns in knee OA population using the Actigraph and the activPAL.

Table 0.3 Summary of studies that measured PA and SB objectively in knee OA patients

Author	Type of study	Knee OA participants	Device used	Country	Outcome of interest	Results
Song et al 2017	Longitudinal	n=545, age=68, female=64%,	GTIM (7days)	USA	MVPA (in 10 min bouts)	
Murphy et al 2016	Cross sectional	n=154,age=65, female=60%, BMI=31	Wrist accelerometer (7days)	USA	PA, PF	MVPA=16.3 mins/day, SB=9.5hrs/day
Liu et al 2016	Cross sectional	n=533,age=65, female=69%, BMI=30	AM-7164 (7days) Household interviews	USA	ST,LPA,MVPA, MVPA (in 10 min bouts)	MVPA=10.8 mins/day, SB=8.8hrs/day, LPA=249 mins/day.
Lee et al 2015	Cross sectional	n=1168,age=55, female=19%, BMI=33	GT1M (7days)	USA	SB, PF	
Semanik et al 2015		n=1168,age=65, female=55%,	GTIM (7days)	USA	ST, WT, MVPA	MVPA=16.3 mins/day, SB=9.8hrs/day
Verlaan et al 2015	Cross sectional	n=30,age=69, female=63%, BMI=30	TriaxialGCdataconcepts (7 days) SQUASH	Netherlands	SC, ST, WT	SC=4402 steps/day, ST = 65% of wake wear time.
Kretzschmar et al 2015	Cross sectional	n=274,age=59, female=52%, BMI=27	GT1M (7days)	USA	MVPA	
Dunlop et al 2014	Cross sectional	n=1680,age=65, female=55%, BMI=30	GTIM (7days)	USA	LPA, MVPA	LPA = 264mins/day

Table 2.3 Continued

Author	Type of study	Knee OA participants	Device used	Country	Outcome of interest	Results
Chmelo et al 2013	Cross sectional	n=160,age=66, female=69%, BMI=33.5	Kenz Lifecorder EX (NL-2200) (7days)	USA	LPA, MPA, VPA, SC	MVPA=8.9 mins/day, SC=6209 steps/day.
Holsgaard-Larson et al 2012	Cross sectional	n=25,age=69, female=49%, BMI=30	SenseWear^{TM}Pro$_2$ Armband	Sweden	SC, EE,	
Semanik et al 2011	Cross sectional	n=139,age=63, female=58%, BMI=33	GT1M (7days) YPAS	USA	LPA, MVPA, bout of MVPA	MVPA=14mins/day, LPA=481 mins/day.
Dunlop et al 2011	Cross sectional	n=1223,age=65, female=50%, BMI=29	GTIM (7days)	USA	ST, LPA,MVPA, MVPA (in 10 min bouts)	MVPA=16.5 mins/day, ST=10hrs/day
Song et al 2010	Cross sectional	n=519,age=62, female=62%, BMI=29	GTIM (7days)	USA	LPA, MPA, VPA	
Farr et al 2008	Cross sectional	n=255, age=55, female=76%, BMI=28	MTI-7164 (7days)	USA	MPA, VPA, MVPA	MVPA = 24.5 mins/day.

SC-Step count, ST-Sedentary time, WT- Wear time, PA-Physical activity, PF-Physical function, LPA-Light physical activity, MVPA-Moderate to vigorous activity, EE-Energy expenditure. The types of accelerometers used (GT1M-, MT1-7164, YPAS, AM-7164) were all uniaxial, SQUASH- Short questionnaire to assess health enhancing physical activity.

Most studies carried out on knee OA populations to determine their PA and SB have looked at the total volume, where overall, outcomes show that knee OA patients are highly sedentary and physically inactive. The outcomes of interest in Table 0.3 also indicate that activity behaviours are mostly measured in total volume except for a few that measured patterns of activity (bouts of MVPA) (Liu et al., 2016; Dunlop et al., 2011b). Accelerometers offer the ability to gain detailed insight into how activity behaviours are accumulated over the day. For example, accelerometers can record hour by hour variation in activity, bouts of activity of 10 minutes as well as the proportions of awake wear time that are spent in activity and in SB on a weekly basis. Understanding how the total volumes of activity are accumulated in knee OA patients and at what hour of a day these accumulations occur is critical in taking the next step of developing and implementing targeted and informed interventions. This detailed information is required as it may help guide care givers to implement necessary interventions so that knee OA patients can receive optimum benefits of exercise on knee function (Liu et al., 2016). Only one study to date has alluded to patterns of activity in knee OA patients being different in the early part of the day (Murphy et al., 2016). Murphy et al (2016) found that the relationship between pain and PA was influenced by patient reported pain-related activity interference and this relationship was evident only in the morning. From the results of this study, the authors suggested needing to determine how best to increase PA in knee OA patients despite their pain levels (Murphy et al., 2016).

The studies described in Table 0.3 have also found that knee OA patients with increased PA usually have reported better functional outcomes (Song et al., 2017; Dunlop et al., 2014). Studies have shown that PA helps in slowing diminishing of muscle strength, physical function and decreasing symptoms of knee OA (Chun et al., 2013; Pietrosimone et al., 2013; Chmelo et al., 2013). In addition, decreasing the amount of time spent in sedentary behaviour is associated with better functional outcome in patients (Lee et al., 2015; Semanik et al., 2015). Lee and colleagues measured sedentary behaviour using the Actigraph GT1M on 1168 knee OA patients

ranging between 49-83 years of age and showed that those with higher sedentary time had worse functional outcomes (Lee et al., 2015). Adults with knee OA who are more sedentary experience a greater loss in functional capacity compared to adults who are less sedentary (Lee et al., 2015; Semanik et al., 2015; Joubert et al., 2007), and this relationship appears to be independent of time spent in moderate to vigorous physical activity (Semanik et al., 2015). Another study measured SB using the Actigraph GT1M on 4796 adults with knee OA between the age of 45 years and 79 years, and showed that a decrease in sedentary time over two years was associated with weight loss that occurred over the same period (Pellegrini et al., 2016). The finding in the latter study has implications for the promotion of weight loss in knee OA patients as this may be a reason why patients become more active and less sedentary. Furthermore, the muscle degeneration that is associated with SB in an ageing population is problematic in knee OA, as the immobility and reduced functionality already experienced due to the knee OA may be exacerbated by the high levels of SB. Greater levels of SB may occur at an earlier age in patients with knee OA, predisposing these patients to an increased risk of sarcopenia as they age (Jefferis et al., 2016). Gianoudis et al (2015) reported that an increase in SB leads to an increased risk of sarcopenia even in healthy elderly populations (Gianoudis et al., 2015). While studies have found associations between habitual physical activity and sedentary behaviour and functional outcomes (as discussed above), few studies have examined the associations between the patterns of activity behaviour and functional outcomes - a gap which the present study addresses.

A comparison between the outcomes of the studies in Table 0.3 is difficult because of the variation in accelerometer brand and methodological processing differences. Furthermore, the degree of severity of symptoms in knee OA differs between almost all the studies. The relationship between knee severity and PA is multifaceted. While most of the studies in Table 0.3 found an inverse relationship between levels of PA and disability, two studies have found that higher levels of PA was associated with an increase in severity of the knee OA (Kretzschmar et al., 2015) or worse functional

outcome (Liu et al., 2016). More studies on the relationship between PA, SB and functional outcome in knee OA need to be done so that greater comparisons can be made between studies that use similar data processing algorithms, severity of disease and outcomes measured (total volume vs. patterns of activity or both).

2.8. Conclusion

Knee OA patients are physically inactive and this is due to the pain which is the main reason for restricting mobility. People with knee OA also achieve a reduction in pain and disability with moderate exercise (Bosomworth, 2009). Physical activity has been approved by the American Geriatric Society (AGS) and the American College of Rheumatology as a prevention and treatment mode for overweight patients with OA of the lower limb (Zhang et al., 2007; Fontaine et al., 2004; Chang et al., 2003). Although increasing PA is beneficial for reducing pain and increasing function in patients with knee OA, the optimal quality of PA promotion (intensity, frequency, duration) has not been defined. The expectation that older adults (including those with knee OA) should take part in 150 minutes of MVPA per week may seem unrealistic in a population with a mobility disorder. Even healthy adults are unable to meet the recommended physical activity guidelines with an approximately 50% prevalence of physical inactivity (WHO 2017). Indeed, literature has shown that the activity levels of knee OA patients are insufficient. Unlike habitual PA though, the number of daily-hours patients with knee OA spend being sedentary (9.8 hours) (Lee et al., 2015) is similar to that reported in healthy adults (9.2 hours) taking part in the European RISC study (Balkau et al., 2008). However, comparing only total volumes of activity may miss the nuances present in the way activity behaviours are accumulated and a richer/more elaborate description of PA and SB patterns is required to better understand and quantify this activity behaviour in patients with knee OA.

In South Africa, the types of patients with knee OA will generally have varying grades of severity of the disease and the relationship between activity levels

(measured objectively) and functional outcomes and quality of life remains not well understood. Currently, no study has described the detailed patterns of how and when PA and SB are accumulated in people with knee OA. To my knowledge no study to date has looked at PA and SB patterns in patients with knee OA in relation to self-reported functional outcomes and quality of life in patients with knee OA. Since pain and early morning stiffness make knee OA patients less active and very sedentary, there may be implications of these symptoms on the variation in daily activity and sedentary behaviour. One question that has not been explored extensively as yet is whether there any hours of the day that PA and SB are worse in knee OA patients? Comprehensive measurements on patterns of PA and SB in this population are needed to answer questions such as the one above and to implement effective interventions aimed at modifying PA levels and SB in patients with knee OA. Knowing the variation in the way knee OA patients move during the day as well as how and when SB is accumulated in this population may advise subtle modifications to activity during the day to allow a more holistic approach to modifying activity behaviour as opposed to a generic total volume change.

CHAPTER 3: METHODS AND MATERIALS

3.1. Participants

Over a period of 12 months, eighty seven males (n=13) and females (n=74) that met the inclusion criteria were between the ages of 45-85 years diagnosed with advanced primary knee OA, based on clinical criteria as defined by the American Rheumatism Association which states that the presence of knee pain with at least three of either age greater than 50 years, stiffness of less than 30 minutes, crepitus, no palpable warmth, bony tenderness or bony enlargement (Altman et al., 1986), were recruited from the Orthopaedics Department of Charlotte Maxeke Academic Hospital Johannesburg. All male and female participants diagnosed with end stage knee OA [Kellgren and Lawrence grades 3 (moderate multiple osteophytes, definite narrowing of joints space, some sclerosis and possible deformity of bone contour) and 4 (large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone contour)] (Kellgren and Lawrence, 1957) and who were scheduled for primary and single total knee replacement surgery between August 2015 and June 2016, were invited to participate in the study. Participants were also included in the study if they were ambulant with or without assistive devices. All participants had been taken off any prescribed medication in the week prior to surgery, which was also the week during which data collection occurred. Participants were excluded if they were wheel chair bound, or had other co-morbidities like musculoskeletal disorders other than the knee OA (e.g. hip OA, rheumatoid arthritis, tendinitis, bone fractures of pelvis and lower limb), neurological diseases (e.g. stroke, dementia, diabetic neuropathy), previous hip and/or knee arthroplasty within the last 12 months and medical disorders (e.g. myocardial infarction) that could significantly affect habitual PA.

3.2. Ethical consideration

A consent form was signed by every participant after having the study verbally explained to them extensively (Appendix F). Participation was voluntary, and participants could withdraw at any time without suffering any repercussions. The

study was approved by the Human Research Ethics Committee of the University of the Witwatersrand (clearance certificate number: M150323 – Appendix E).

3.3. Study Design and Procedure

The study was a cross-sectional design. Participants were taken off their medication approximately one week before their scheduled surgery. All assessments were conducted during the week that participants were off their medications. Participants were asked to complete knee functional outcome and quality of life questionnaires as well as questionnaires on their health and socio-economic status (SES). Two accelerometer devices were then fitted to each patient for one week before their scheduled total knee replacement surgery. Participants were asked to wear the accelerometers for 24 hours a day for a period of seven days. After seven days of accelerometer wear, both accelerometers were collected at the next possible visit to the hospital or arrangements were made for collection from participants at a location most convenient to the participant.

All male and female patients diagnosed with advanced knee OA and who were scheduled for primary and single total knee replacement surgery and attending the clinic in the Division of Orthopaedics at the Charlotte Maxeke Academic Hospital in Johannesburg between August 2015 and June 2016 were recruited.

3.4. Instrumentation and outcome measures

3.4.1. Anthropometric measurements

Height and weight were measured to the nearest millimetre, and gram, respectively, using an electronic scale (Dismed, USA) and a stadiometer (Seca, model 202, Germany). Body mass index (BMI) was calculated from the height and the weight (weight/square of height) for each participant.

3.4.2 General health questionnaire

A general health questionnaire (Appendix A) was used to record average wake and sleep time on weekdays and weekends, history of knee OA, drug and tobacco use and any co-morbidities. A household amenity questionnaire was used to determine the socioeconomic status (SES) of each participant. The amenity questionnaire gave a list of general household items (washing machine, indoor toilet, computer, television etc.) and the participant was asked to indicate the items that they owned (Appendix A). A score was then assigned to each participant (sum of items owned) to calculate an amenity score, which was used to categorise their socioeconomic status. Their sleep pattern was also recorded (i.e. times they wake from sleep and time they go to sleep during weekdays and weekends). It should be noted that this set of questions were not derived from any set of questionnaires.

3.4.1. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

The WOMAC index is a widely used self-report questionnaire with 24 items used to assess joint pain, stiffness and physical functioning of patients with knee and hip OA (Appendix B). The 24 items are divided into 3 subscales: Pain subscale: 5 items; physical function subscale: 17 items and a stiffness subscale: 2 items. Every participant was required to answer each question with a score of between 0 and 4 with 4 being most severe. These items request the respondent to indicate the degree of pain, stiffness and physical functioning while engaging in specific activities, including walking, going upstairs, in bed at night, sitting and standing upright. The scores for the subscales are summed up to obtain a total score. The total WOMAC score is 96 (100%) (accounted for by 20, 8 and 68 subtotal scores of pain, stiffness and ADL subscales respectively). Higher scores indicate more pain, stiffness and decreased or impaired physical function. Thus, a score of 96 (100%) represents worst possible outcome and 0 represents no impairments or best possible state. Reliability and validity of WOMAC has been established in evaluating the severity of knee OA

in populations from different countries (Mehta et al., 2016; Tüzün et al., 2005; Salaffi et al., 2003; Escobar et al., 2002). It should also be noted that all participants were taken off medication for pain when the WOMAC questionnaire was filled.

3.4.2. Knee injury Osteoarthritis Outcome Score (KOOS)

The KOOS questionnaire assesses pain, daily living function, recreation function, sport function, and knee related quality of life (five subscales), by using a five point Likert scale to acquire a response from patients on the above five subscales (Appendix C) (Xie et al., 2007; Roos and Lohmander, 2003). Each subscale asks about the frequency (never to always) or severity (none to extreme) of symptoms experienced. Reliability and validity of the KOOS in evaluating the intensity of knee OA has been established in different countries (Nakamura et al., 2011; de Groot et al., 2008; Ornetti et al., 2008). All participants were taken off pain medication a week before they answered the KOOS questionnaire.

3.4.3. UCLA (University of California Los Angeles) activity index

This is a 10-point investigator-rated scale (1-10 with 1 indicating wholly inactive and 10 being regularly participates in contact sports) and is a convenient tool in assessing patient's activity levels (Appendix D). The UCLA has been validated and found to be reliable in assessing knee OA patients activity levels (Saleh et al., 2005).

3.5. Habitual physical activity and sedentary behaviour measurements

3.5.1. Actigraph

The Actigraph GT3X+ accelerometer (Actigraph, LLC, Fort Walton Beach, FL, USA) was worn by participants for 24 hours/day for seven days. The Actigraph was attached to an elastic belt which the participants wore around the waist on the same side of the knee affected by OA. Participants were instructed to remove the Actigraph when bathing or swimming (any water activity). The Actigraph was set to record at a

frequency of 30 Hz and vertical axis data were reduced to 60 second epoch data. Data were then processed for sleep and non-wear times using a custom built and validated semi-automated algorithm (McVeigh et al., 2016). Where distinct sleep times could not be obtained, sleep periods were obtained from the reported sleep and wake times recorded on the general health questionnaire and were manually removed from the data. Non-wear time was classified as two minute intervals with consecutive zero counts per minute for a minimum of 90 minutes (with an allowance of up to two minutes of counts between zero and 50) (Choi et al., 2011). Sleep and non-wear periods were removed from the data, leaving only daily waking wear time. For a day to be classified as valid, a minimum wear time of 10 hours (600 minutes) was required (Figure 0.1). Only participants with four or more valid days of Actigraph wear were included for data analysis (Mâsse et al., 2005). Each 60 second epoch of final accelerometry data was classified according to calibration equations validated for the Actigraph (Freedson et al., 1998). Light physical activity and MVPA were defined as less than 1951 counts per minutes and between 1952 – 5724 counts per minutes, respectively (Freedson et al., 1998). Time spent in sedentary behaviour was estimated as the amount of accrued time spent below 100 counts per minute recorded during wake wear time (Matthews et al., 2008). Total volumes of activity in the different intensities (i.e. sedentary, light and MVPA) as well as patterns of activity (i.e. bouts of time spent in each activity intensity) were the variables that were derived from the waking wear data. Notably, the Actigraph has been shown to have poor validity at slower walking speeds which has implications for its use in a population with a musculoskeletal disorder (Riel et al., 2016)

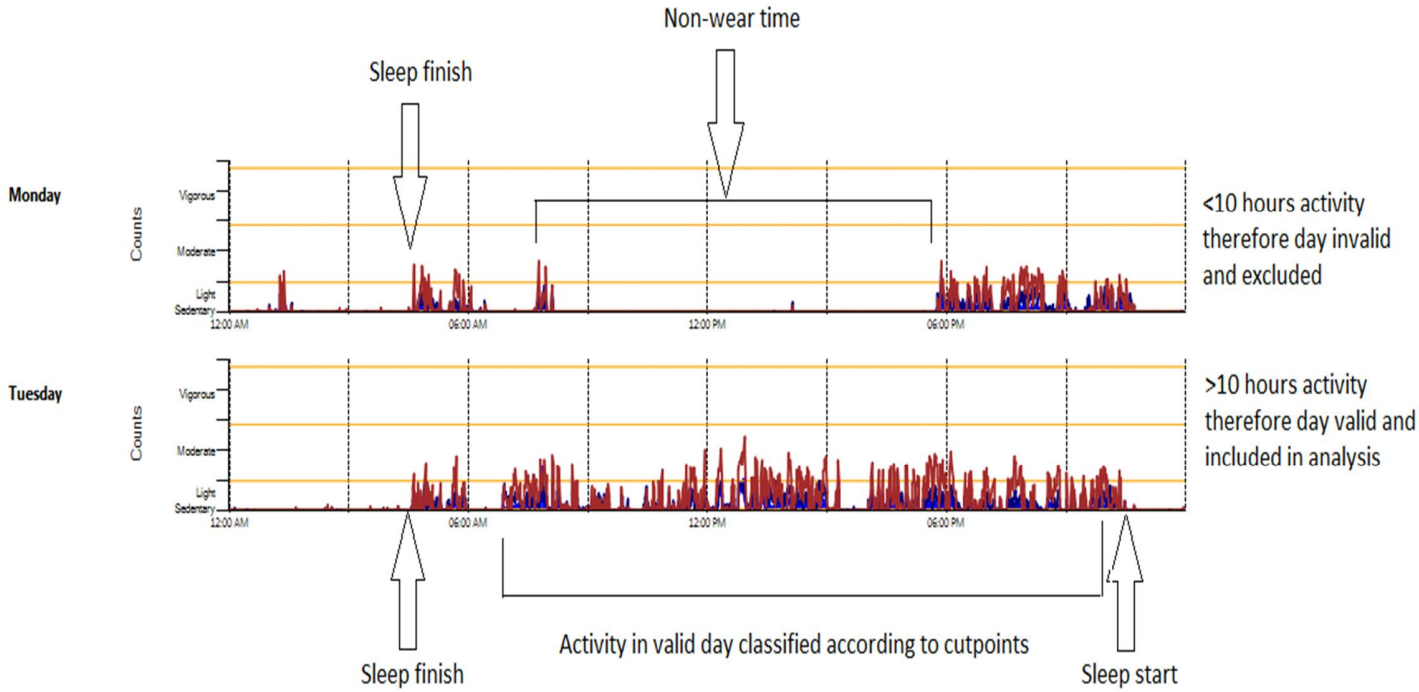


Figure 0.1 Schematic of output from the Actigraph

3.5.2. The activPAL accelerometer

The activPAL (Physical Activity Technologies, Glasgow, Scotland) was taped to the anterior thigh of the participant with waterproof taping and the participant was asked to keep the activPAL on for the same amount of time as the GT3X+ (24 hours/day, seven days). Because the activPAL was waterproofed it did not need to be removed during water activities. The activPAL was collected at the same time as the Actigraph and data were downloaded and analysed. Data were downloaded in 15s epochs. Waking wear data were again extracted using a validated algorithm (Winkler et al., 2016). Briefly, the activPAL events files were used to provide the required data for input to the algorithm. Sleep/non-wear periods were removed first from any 24 hour period in the data and the remaining data were referred to as the waking wear data. Invalid days or days with insufficient data were then removed based on the following criteria: if the day contained any one activity that accounted for ≥ 95% of waking wear time, or, < 500 steps or < 10 hours of waking wear. The remaining data were then visually checked against diaries and as well as by checking the activity graph output from the activPAL software itself (Figure 0.2). If the participant reported the activPAL falling off, all data were excluded. A minimum of three valid days were required for inclusion into final analysis as compliance with activPAL wear was better because the device was taped onto the participant with less likelihood for removal compared to the Actigraph (Trost et al., 2005). There was no need to remove non-wear because the activPAL is taped on so either it fell off in which case all data were excluded or it didn't in which case there is no non-wear to remove. The activPAL data provided information about the start time and duration of each sitting, lying, standing and stepping bout. Total sedentary time per day was determined by summing the duration of all sitting/lying bouts and averaging it over the number of days the device was worn. An interruption or break from sedentary time was indicated at points where a sitting/lying bout was followed by a standing or stepping bout.

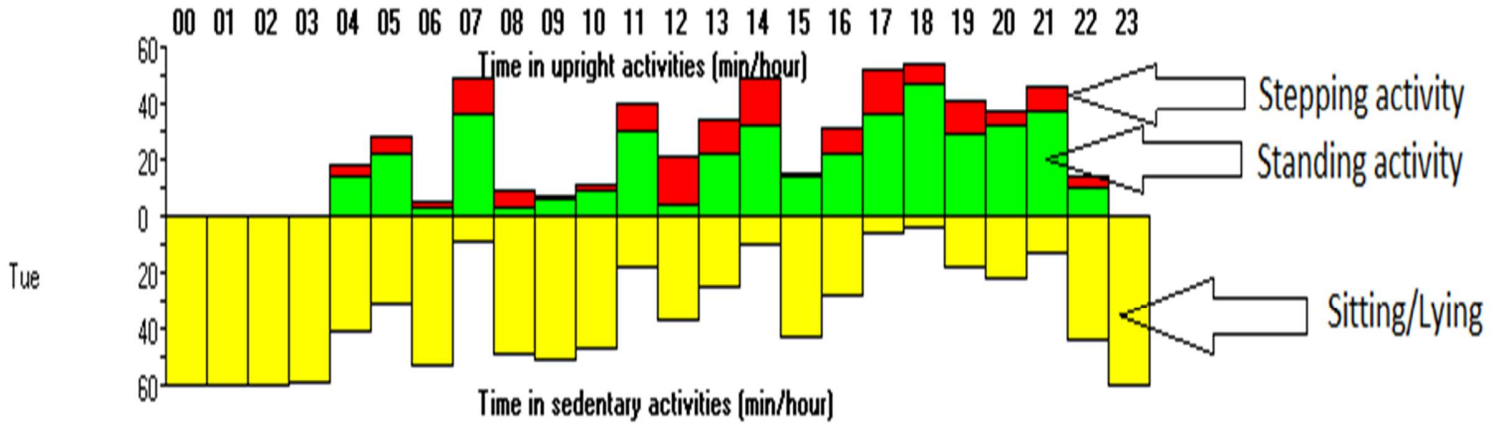


Figure 0.2 Schematic of output from the activPAL

3.6. Data Analyses

Means (SD) or median (range) were used to summarise data for descriptive characteristics of participants while mean and (95% CI) was reported for total volumes and patterns of activity behaviour. Scores for the WOMAC and KOOS were calculated by their respective scoring systems. Exposure variation analysis was used to describe the proportions of time spent in bouts of activity of differing lengths. Hour by hour variation in sedentary time over the day was analysed using generalised linear mixed models because the data was not normally distributed. This model included all data on valid days and was adjusted for compositional differences in the hourly data provided by the patients in the sample. Adjustment for multiple comparisons was made using the Sidak method. From this model, differences between the hour of the day and the grand mean are reported. A partial correlation (adjusted for total awake wear time, gender, BMI, age and smoking history) was performed to determine whether a relationship existed between KOOS and WOMAC scores with total and patterns of activity behaviour. Correlations were classified as weak (0.2-0.4), moderate (0.5-0.7) or strong (0.8 and above). MVPA was not normally distributed therefore MVPA was log-transformed and adjusted for total awake wear time, gender, BMI, age and smoking history. The standardised predicted values were then correlated with the KOOS and WOMAC scores (Spearman's rank correlation for non-normal distributions) to determine the relationship between MVPA and functional outcome. For further analysis, spydergrams were used to describe z-scores calculated based on the median of the scores obtained from the WOMAC pain and activities of daily living sub-scales. Participants were then grouped as either having a score above the median or below the median. The activity behaviours and patterns were then compared between the two median groups using a multivariate linear model adjusting for total awake wear time, gender, BMI, age and smoking history and correcting for multiple comparisons using the Sidak method. IBM SPSS (version 24, SPSS Inc., Chicago, IL, USA) and SAS (v 9.4, SAS Institute, Cary, NC, USA) was used for all analyses. A p value of <0.05 was considered significant

CHAPTER 4: RESULTS

A total of 87 participants met the inclusion criteria and were recruited into the study. Of these, 11 did not meet the minimum wear criteria for the Actigraph and 22 for the activPAL. Therefore, complete Actigraph data were available for 76 participants and 65 participants had complete activPAL data.

4.1. Demographics and anthropometric characteristics

The demographic and anthropometric characteristics of all participants recruited for the study are shown in Table 0.1. The participants had a mean (SD) age of 65.0 (8.8) years, were mostly women and most were classified as being obese with an average BMI of 34.4 (7.8) kg/m^2. Participants' functional score as determined from WOMAC and KOOS knee questionnaires indicated that they had poor function (WOMAC pain, stiffness and ADL subscales maximum scores possible were 20, 8 and 68 respectively while KOOS pain, stiffness, ADL, sport and recreation and quality of life subscales maximum scores possible were 36, 28, 68, 20, and 16 respectively). Participants took part in little or no activity (mean score on the UCLA index of 2.4 out of a possible score of 10).

Table 0.1 Characteristics of study participants

	Total (n=87)	Male (n=13)	Female (n=74)
Age (years)	65.0 (8.8)	66.6 (9.6)	64.7 (8.7)
Body mass (kg)	86.1 (21.1)	95.8 (24.2)	84.4 (20.2)
Height (m)	1.6 (0.1)	1.7 (0.1)	1.6 (0.1)
BMI (kg/m^2)	34.4 (7.8)	33.8 (7.2)	34.4 (7.9)
Smoker (%)	8 (9)	4 (31)	4 (5.4)
Asset indicator score	10 (3)	12 (2)	10 (3)
Educational Status (n (%))			
Below Secondary School	63 (72)	7 (54)	56 (76)
Completed Secondary School (Grade 12)	10 (12)	4 (31)	6 (8)
Tertiary Education	14 (16)	2 (15)	12 (16)
Ethnicity (n (%))			
Black	59 (68)	1 (8)	58 (78)
Caucasian	28(32)	12 (92)	16 (22)
WOMAC			
Stiffness	6 (8)	5 (8)	6(8)
Pain	15 (20)	10 (16)	15 (15)
ADL	50 (64)	40 (51)	52 (46)
KOOS			
Stiffness	20 (23)	15 (19)	20 (22)
Pain	27 (34)	20 (29)	28 (20)
ADL	49 (64)	38 (52)	51 (48)
Sport and recreation function	20 (9)	18 (9)	20 (6)
Quality of life	13 (11)	13 (9)	14 (9)
UCLA	2 (5)	2 (5)	2 (5)

Data presented as mean (SD) except for knee function scores and UCLA (University of California Los Angeles) score which are median (range), and gender, smoking, educational status, and ethnicity in

number (percentage). BMI – Body mass index. A higher score for WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) pain, stiffness and ADL (Activity of daily living) subscales (maximum scores possible were 20,8, 68 respectively) and KOOS (Knee injury Osteoarthritis Outcome Score) pain, stiffness, ADL, sport and recreation and quality of life subscales (maximum scores were 36, 28, 68, 20, and 16 respectively), indicates a worse outcome.

4.2. How physically active and sedentary are patients with advanced knee OA?

4.2.1. Actigraph GT3X+

Total volumes of activity behaviour as well as the number of breaks taken from sedentary behaviour measured using the Actigraph are shown in Figure 0.. Participants spent approximately 70.0% of their wake wear time in sedentary behaviour, 28.9% in light activity, and 0.9% in MVPA. On average, participants accumulated (mean (SD) 48.7 mins (134.3)) of MVPA over the week that they wore the monitor for. The number of steps and number of breaks in sedentary behaviour were recorded as mean (SD) 3556 (2650) steps/day, and 85(22) breaks/day respectively.

Table 0.2 Physical activity and sedentary time as measured with the Actigraph (AG)

	All (n = 76)	Women (n = 63)	Men (n = 13)
Waking wear time, hrs/day	15.6 (15.1-16.0)	15.8 (14.8-16.7)	15.5 (15.0-16.1)
Sedentary time, hrs/day	10.9 (10.5-11.4)	11.6 (10.6-12.5)	10.8 (10.3-11.3)
Light activity, hrs/day	4.5 (4.1-5.0)	4.1 (3.2-4.9)	4.6 (4.1-5.1)
MVPA, mins/day	8.2 (3.3 - 13.0)	5.0 (0.5 - 9.4)	8.8 (3.0 - 14.6)
Sedentary, % of waking wear	70.6 (67.8-73.3)	73.7 (68.7-78.6)	69.9 (66.8-73.1)
Light activity, % of waking wear	28.6 (26.1-31.1)	25.8 (21.0-30.6)	29.2 (26.3-32.1)
MVPA, % of waking wear	0.8 (0.3-1.3)	0.5 (0.06-0.1)	0.9 (0.3-1.5)
Prolonged sedentary time (in ≥30 min bouts), hrs/day	4.1 (3.6-4.6)	4.1 (2.9-5.4)	4.1 (3.5-4.7)
All waking wear time, cpm	486.5 (440.6 – 532.4)	488.2 (435.0 – 541.4)	478.2 (390.2 – 566.2)
Sedentary time, cpm	11.2 (10.3 – 12.1)	11.3 (10.3 – 12.3)	10.6 (8.4 – 12.8)
Light activity, cpm	439.2 (410.0 – 468.3)	438.3 (405.3 – 471.3)	443.3 (375.3 – 511.3)
MVPA, cpm	2608.4 (2500.8 – 2716.1)	2630.2 (2497.9 – 2762.5)	2519.5 (2415.9 – 2623.1)
Meet MVPA recommendation	7 (9)	6 (10)	1 (8)

Data in mean (95% CI), except meet MVPA recommendation represented in number/%. MVPA - moderate to vigorous physical activity, cpm - counts per minutes.

4.2.2. The activPAL

According to the activPAL data shown in Figure 0., participants were awake for 16 hours of the day of which 60.0% was classified as being spent sedentary. Standing and stepping time accounted for 32.0% and 8.2% of awake wear time respectively.

Table 0.3 activPAL derived measures of activity and sedentary behaviour

	Total (n=65)	Male (n=12)	Female (n=53)
Sitting time (hrs/day)	9.3 (8.5 – 10.1)	11.6 (9.9-13.2)	8.8 (7.9-9.6)
Standing time (hrs/day)	5.0 (4.4 – 5.6)	3.2 (2.3-4.0)	5.4 (4.8-6.1)
Stepping time (mins/day)	76.5 (66.6 – 86.3)	58.9 (43.6-74.3)	81.3 (69.6-92.9)
Steps (number/day)	2489.0 (2130.3 – 2847.7)	1952 (1353-2551)	2642 (2220-3064)
BST (number/day)	54.5 (12.7-221.7)	52.6 (21.6-99)	54.9 (12.7-221.7)

Data are presented as mean (95% CI). BST – break in sedentary time.

4.3. How do the patterns of physical activity and sedentary behaviour differ over the course of the week and day?

The accumulation of daily activity behaviour (sedentary, light activity, MVPA) in bouts of different durations is shown in Figure 4.1. The dominance of sedentary time over other intensities is highlighted in the figure, as is the dominance of short bouts of light and moderate intensity activity.

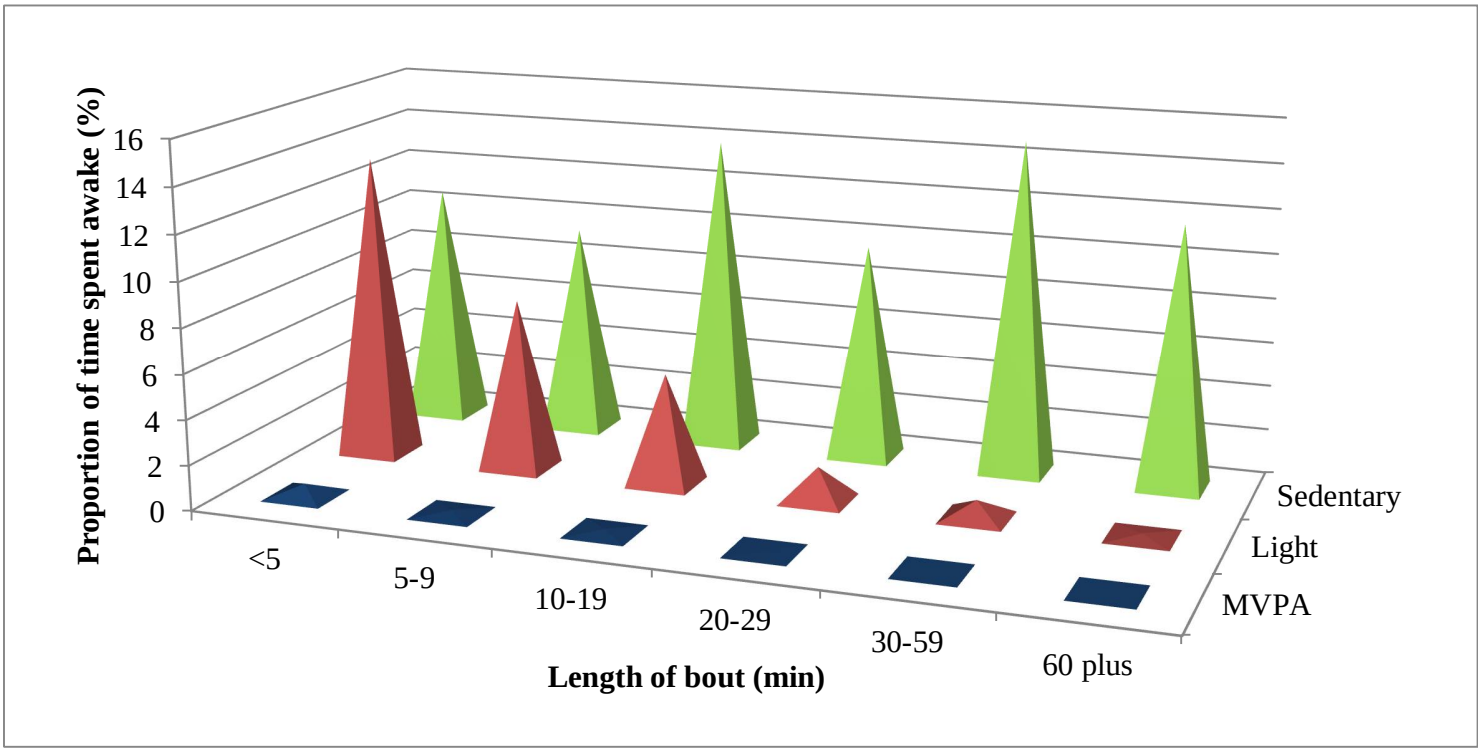


Figure 0.1 Accumulation of PA and SB in bouts of differing durations. Data are presented as the proportion of the time spent awake in each bout category. Data were measured using the ActiGraph device. MVPA – moderate to vigorous physical activity (blue blocks), light physical activity (red block), sedentary activity (green block).

Participants spent the greatest proportion of their awake wear time in bouts of sedentary behaviour lasting between 30 and 59 minutes i.e. they spent most of their sedentary behaviour sitting/lying for more than 30 minutes at a time. On the other hand, when the participants took part in light activities, the majority of these bouts lasted less than 5 minutes. Only 0.5% of the participants' total awake wear time was spent doing moderate-vigorous intensity exercises lasting less than 5 minutes.

Figure 0.2A and B show the variation in sedentary behaviour and light activity over the course of the day compared to the mean of each of those activities over the whole day (data taken from 6 am to 10 pm). Participants were significantly less sedentary between 6 am and 9 am compared to the grand mean of sedentary time per hour over the day (39.5 (15.2) min/hr; $p<0.01$) and were significantly more sedentary per hour from 3 pm to 7 pm ($p<0.05$) (Figure 0.2A). Participants appeared to be less sedentary at 10 pm ($p=0.006$) compared to the mean over the day. Figure 0.2B shows that participants took part in significantly more light activity in the morning (between 7 am and 11 am; $p<0.01$), however, they became less lightly active over the day and were significantly less so between 6 pm and 10 pm ($p<0.01$; grand mean of light activity over the day was mean (SD) 17.0 (13.4) min/hr).

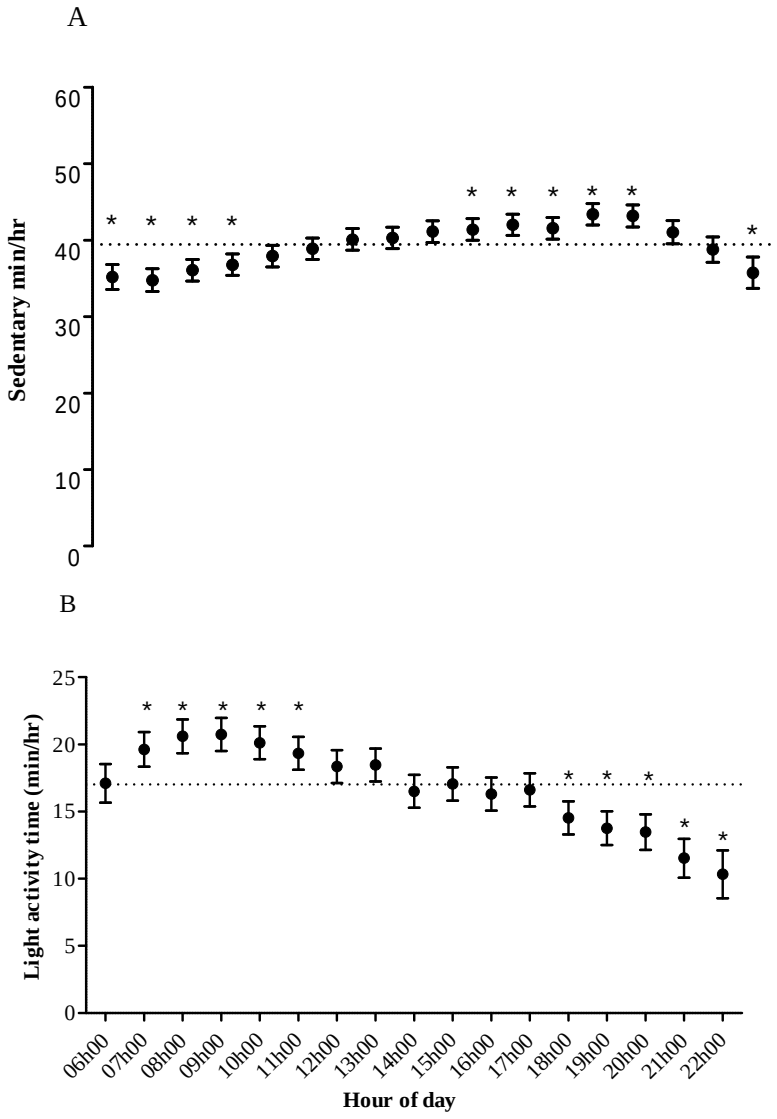


Figure 0.2 Hour by hour variation in sedentary behaviour and light physical activity - A) Hour by hour variation in sedentary behaviour (Actigraph GT3X+ data). Data are minutes spent in sedentary behaviour per hour (and Sidak adjusted 95%CI) for each hour of the day vs the grand mean*$p<0.05$ (grand mean is represented by dotted lines in diagrams A and B). B) Hour by hour variation in light physical activity (Actigraph GT3X+ data). Data are minutes spent in light physical activity per hour (and Sidak adjusted 95% CI) for each hour of the day vs the grand mean*$p<0.05$.

4.4. Is objectively measured physical activity and sedentary behaviour associated with functional capacity/outcomes as assessed by self-report questionnaires?

4.4.1. Actigraph

There was a significant correlation between physical activity, sedentary behaviour variables and scores obtained from the WOMAC questionnaire, pain and ADL subscales (Table 4.4). WOMAC pain scores were significantly correlated with time spent in sedentary behaviour (p=0.022) and light physical activity (p=0.043). WOMAC pain scores were also correlated to the number of steps (p=0.020), the number of breaks in bouts of SB greater than 20 minutes (p=0.016) and the average duration of breaks in SB (p=0.024). Similarly, WOMAC ADL scores were significantly correlated with time spent in sedentary behaviour (p=0.023), time spent in light physical activity (p=0.048) and number of steps (p=0.010). All correlations, although statistically significant, were considered weak.

Table 0.4 Correlation matrix between KOOS and WOMAC scores and total and patterns of activity behaviours measured using the Actigraph

	KOOS					WOMAC		
	Stiffness	Pain	ADL	SR	QOL	Stiffness	Pain	ADL
Sedentary time	0.034	0.087	0.196	0.001	0.141	-0.003	0.277*	0.245
LPA	-0.008	-0.077	-0.185	-0.016	-0.124	0.022	-0.240*	-0.206
MVPA	-0.028	0.112	-0.019	0.109	0.008	0.066	-0.109	-0.118
No. of steps	0.005	-0.075	-0.186	-0.050	-0.145	-0.070	-0.282*	-0.286*
No. of breaks in SB	0.063	-0.058	-0.112	-0.083	-0.099	-0.082	-0.095	-0.191
No of breaks in bouts of SB >20	-0.115	-0.073	-0.145	0.080	-0.101	-0.024	-0.292*	-0.167
Time in bouts of SB > 30	-0.057	0.043	0.133	0.115	0.091	-0.039	0.155	0.200
Average duration of breaks in SB	-0.055	-0.081	-0.189	0.019	-0.104	-0.024	-0.277*	-0.178
Average duration of sedentary bouts	-0.016	0.108	0.150	0.113	0.167	0.082	0.184	0.207
Average duration of light activity bouts	-0.005	-0.059	-0.161	-0.022	-0.073	0.061	-0.185	-0.094

Values are partial correlation coefficients adjusted for gender, BMI, smoking, age, and total awake wear time. * $p<0.05$; **$p<0.01$. LPA = light physical activity; MVPA = moderate-vigorous physical activity; SB = sedentary behaviour. MVPA was log-transformed.

4.4.2. The activPAL

There was a significant correlation between activPAL stepping time with KOOS ADL (p=0.004) and QoL (p=0.008) scores. There was also a significant relationship between stepping time and WOMAC pain (p=0.01) and WOMAC ADL (p=0.02) scores. Sitting time was significantly correlated with WOMAC pain (p=0.02) (Table 4.5). Again all correlations, although statistically significant, were considered weak.

Table 0.5 Correlation matrix between KOOS and WOMAC scores and activity behaviours measured using the activPAL

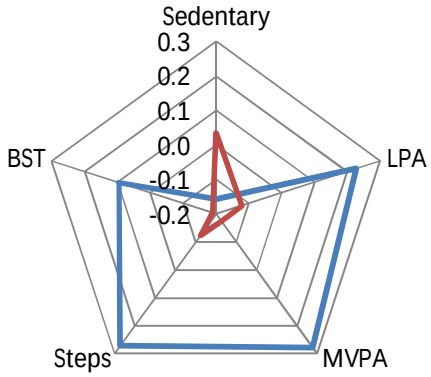
	KOOS					WOMAC		
	Stiffness	Pain	ADL	SR	QOL	Stiffness	Pain	ADL
Sitting time	0.030	0.179	0.295*	0.034	0.211	0.089	0.299*	0.262
Standing time	-0.090	-0.119	-0.150	0.151	-0.135	-0.175	-0.265	-0.172
Stepping time	-0.154	-0.111	-0.276*	-0.020	-0.271*	-0.123	-0.299*	-0.309*
Steps	-0.134	-0.091	-0.263*	-0.053	-0.248	-0.081	-0.276*	-0.319*

Values are partial correlation coefficients adjusted for gender, BMI, smoking, age, and total awake activity time. *p<0.05; **p<0.01.

Figure 0.3 (A and B) represent z-scores of different activity behaviours of patients classified as having WOMAC pain subscale z-scores above or below the median of the group. Participants with scores below the median (i.e. better pain) shown by the blue line, appeared to be less sedentary and take part in more MVPA compared to participants with scores above the median (i.e. worse pain) (Figure 0.3A). However, these differences were not significant.

Figure 0.3B shows that when the group below the median (i.e. better pain) had a break from sedentary behaviour, the average duration of that break (represented as BST dur in the graph) was longer compared to those participants with WOMAC pain scores above the median (worse pain) ($p=0.046$). There were no differences between groups above and below the median in terms of the number of breaks from sedentary behaviour bouts lasting longer than 20 minutes ($p=0.06$), time in sedentary bouts of greater than or equal to 30 minutes ($p=0.21$), the average duration of sedentary bouts ($p=0.15$) or the average duration of breaks from SB into light ($p=0.19$) or moderate to vigorous ($p=0.18$) activities.

A.



B.

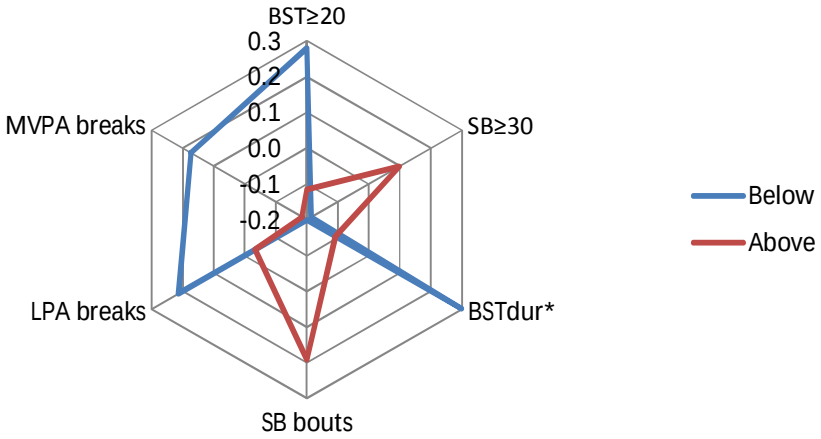
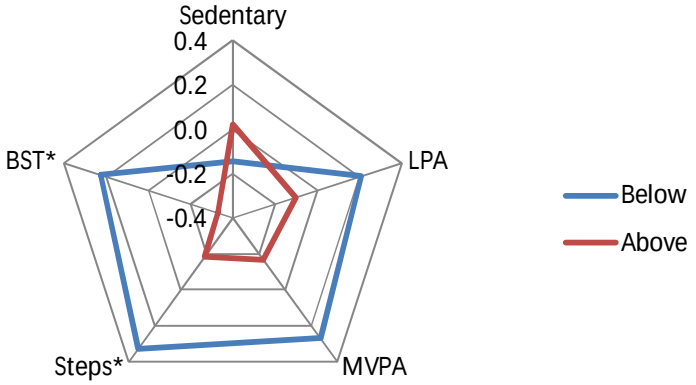


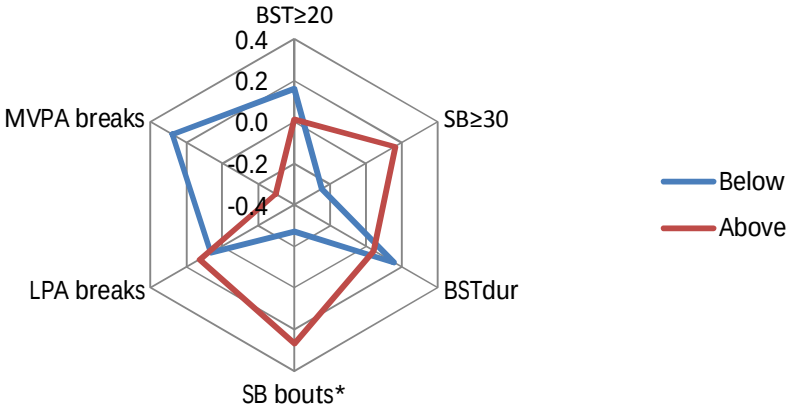
Figure 0.3 Spydergrams of z-scores based on WOMAC pain scores - **A**) total volumes of activity, breaks in sedentary behaviour (BST) and number of steps. **B**) patterns of activity behaviours of patients classified as being above or below the median WOMAC pain subscale z-score. In figure B, BST≥20 = breaks from sedentary behaviour bouts lasting longer than 20 minutes; SB≥30 = time in sedentary bouts of greater than or equal to 30 minutes; BSTdur = average duration of breaks from sedentary behaviour; LPA breaks = average duration of the breaks from SB into LPA; MVPA breaks = average duration of the breaks from SB into MVPA. *p<0.05.

Figure 0.4 (A and B) represent z-scores of different activity behaviours of patients classified as having WOMAC ADL subscale z-scores above or below the median of the group. Participants with scores below the median (i.e. better function) shown by the blue line, had a significantly greater number of steps (p= 0.03) and had a greater number of breaks in sedentary time per day (p=0.017) (Figure 0.4A).

Figure 0.4B shows that the group below the median (i.e. better function) had a shorter duration of sedentary behaviour bouts (p= 0.029).



A.



B.

Figure 0.4 Spydergrams of z-scores based on WOMAC ADL scores - **A**) Total volumes of activity, breaks in sedentary behaviour (BST) and number of steps. **B**) Patterns of activity behaviours of patients classified as being above or below the median WOMAC ADL subscale z-score. In figure B, BST≥20 = breaks from sedentary behaviour bouts lasting longer than 20 minutes; SB≥30 = time in sedentary bouts of greater than or equal to 30 minutes; BST dur = average duration of breaks from sedentary behaviour; LPA breaks = average duration of the breaks from SB into LPA; MVPA breaks = average duration of the breaks from SB into MVPA. *p<0.05.

CHAPTER 5: DISCUSSION

This study was carried out to describe the patterns of physical activity (PA) and sedentary behaviour (SB) using objective methods (Actigraph and activPAL) and to assess physical function and health outcomes using self-reported questionnaires in relation to objectively measured activity behaviour in patients with advanced knee OA. This study showed that knee OA patients are physically inactive (not meeting the recommended 150 minutes per week guidelines), highly sedentary (mostly in bouts lasting 30 minutes or more), and participate in low levels of light physical activity mostly in bouts lasting less than five minutes at a time. The majority of sedentary time was accumulated in the later part of the day. Other findings include the significant correlation between self-reported pain and function with objectively measured patterns of activity. Higher self-reported pain in the affected knee was related to lower levels of objectively measured total volume of activity (LPA and MVPA) as well as fewer steps during the day and less time in stepping activities. Higher pain scores were also related to more unfavourable patterns of SB, where high scores were associated with taking fewer and shorter duration breaks from prolonged SB bouts (> 20 minutes). Patients reported worse outcomes for pain and activities of daily living also experienced a higher sitting time as measured using the activPAL.

Previous studies have used the Actigraph device to objectively assess physical activity in patients with knee OA (Dunlop et al., 2011b; Semanik et al., 2011). The present study however, is one of a few to date that has used the activPAL accelerometer in addition for the assessment of physical activity and sedentary behaviour in patients with knee OA. Although the purpose of the present study was not to compare the monitors, the study has shown that both monitors were effective in describing the habitual activity and sedentary behaviour of patients with knee OA and that these measures were related to the pain and activities of daily living indices reported using subjective questionnaires most commonly used in knee OA.

How physically active and sedentary are patients with advanced knee OA?

Results from this study showed that about 70% of awake wear time of Actigraph data and 60% of awake wear time of activPAL data were spent being sedentary. There is poor data available in South Africa on the prevalence on inactivity in adults however the latest South African Health and Nutrition Examination Survey (SANHANES 2012), states that 28 and 45% of men and women, respectively, are considered unfit. One cannot assume that being fit is related to participation in sufficient physical activity however using this data we presume that the adults with knee OA in our study were relatively inactive compared to the general population of South African men and women. Findings from previous studies in knee OA patients have reported sedentary levels of 62% (Liu et al., 2016), and 67% (Lee et al., 2015) of wake wear time. The differences may be attributed to the use of a different accelerometer as well as self-identification of early stage knee OA in other study participants (Liu et al., 2016). The participants in the present study were in end stage knee OA therefore they may have been more symptomatic and may have experienced more limitations to movement. Lee and colleagues (2015) on the other hand reported 67% of awake wear time spent in sedentary behaviour, in patients either at risk of knee OA or at an early stage of the disease. The participants with end-stage knee OA are more likely to be more sedentary because their symptoms (e.g. pain, stiffness) are likely to be more severe thereby making them less active and more sedentary. Measuring sedentary behaviour is important because it has been implicated in increasing waist circumference (Healy et al., 2008), reducing physical function (Seguin et al., 2012) and also increasing risk of sarcopenia (Gianoudis et al., 2015). Dunstan and colleagues (2005) used self-report method to find a strong association between sedentary time and metabolic risk (Dunstan et al., 2005). Therefore, not only are knee OA patients sedentary, they are also at risk of other life style diseases (metabolic diseases) because they record very high levels of sedentary time.

The results from my study also showed that the average number of steps per day recorded from the Actigraph and activPAL data were 3556 and 2489 respectively. Three previous studies have measured step count in knee OA patients using

accelerometers (Lützner et al., 2014; Hurley et al., 2012; Tonelli et al., 2011). One of the studies used an activPAL monitor (Tonelli et al., 2011) and recorded 4726 steps in their participants who had a mean age and BMI of 61 years and 35.5 kg/m^2, respectively. Lützner et al (2014) also used an activPAL accelerometer, in 97 knee OA patients before total knee replacement and recorded 5278 steps per day. Although they had a similar mean age (68 years) with my study, their mean BMI (31kg/m^2) was slightly lower than my study's participants which could be the reason for the greater number of steps recorded. The last study used a pedometer and reported a step count of 5740 per day (Hurley et al., 2012). Their high values could be attributable to the fact that their inclusion criteria were that patients had to meet a moderate classification based on (1) their self-reported ability to perform 3 functional tasks (jog 5m, walk a city block, and walk up a flight of 10 stairs in a reciprocal manner), and (2) that they were not on a wait list for total knee arthroplasty. Notably, the Actigraph has been shown to have poor validity at slower walking speeds which has implications for its use in a population with a musculoskeletal disorder (Riel et al., 2016).

In the present study, knee OA patients took part in 270 mins/day of light physical activity and 8 mins/day of moderate to vigorous activity respectively. From previous studies measuring activity in knee OA patients, 131 mins/day (Chmelo et al., 2013), and 250 mins/day (Liu et al., 2016) have been reported for LPA. In the study by Chmelo et al (2013) who used a Kenz lifecorder EX (NL-2200) a uniaxial accelerometer, their sample was drawn from the Intensive Diet and Exercise for Arthritis (IDEA) study (Messier et al., 2009) whose participants had a mean age of 66 years and a mean BMI of 33.5 kg/m^2. One of the inclusion criteria in the Messier study was recruiting a population with a specific sedentary lifestyle, defined as not participating in a program that incorporates more than 30 minutes per week. This may be an explanation for the lower LPA levels compared to the present study. Liu and colleagues (2016) used an AM-7164 accelerometer in their study and reported knee OA patients with a mean age of 65 years taking part in an average of 248.5 mins/day

of light physical activity, which was similar to my study (270 mins/day). However, their participants self-identified their knee OA, which could be attributable to the slightly lower level of LPA. Furthermore, only 8.8% of participants in the current study met the PA guidelines which are ≥150 mins/week of MVPA. Previous studies show that 6% - 17% of knee OA patients studied met the recommended PA guidelines (Liu et al., 2016; Harding et al., 2014; Lee et al., 2013; Semanik et al., 2011). Using self-reported PA, two other studies have (Dunlop et al., 2011b; Hootman et al., 2003) reported between 15 and 40% of knee OA patients, achieving the recommended PA guidelines. However, studies that have assessed MVPA in healthy older adults have shown that only about 10-15% of older adults meet the recommended guidelines of 150 minutes per week of MVPA (Jefferis et al., 2014; Tucker et al., 2011). The severity of disease, age of the population studied as well as the BMI of the patients could influence the levels of PA and SB and should be considered when investigating activity behaviours in knee OA. Performing an average of 150 minutes of MVPA per week may be a difficult task for patients with end-stage knee OA, especially as they are very sedentary secondary to pain, have deformities of the knee and high BMI, all of which decrease functional ability. The fact that total volumes of activity appear to not be different between healthy and diseased populations, suggests that subtleties in activity behaviours may be what distinguishes how active or inactive knee OA patients are compared to the normal population.

How do the patterns of physical activity and sedentary behaviour differ over the course of the week and day?

Another important aspect of this study is the fact that it also used objective methods to assess the patterns of sedentary behaviour and physical activity. These data give insight into how SB, light activity and moderate to vigorous activity are being accumulated during the day in patients with knee OA. The importance of knowing how patients accumulate these activities may help improve overall quality of life by taking part in activities of daily living that their knee OA may not allow for, for

example shopping, walking, cooking. Most of the participants in the present study were sedentary in longer bouts (i.e. in bouts between 30 minutes to one hour). It also showed that light physical activity was accumulated during the day in very short bouts (mostly in bouts less than five minutes) while very little MVPA was done. Ideally patterns of activity should show activity (light activity, or moderate to vigorous activity) accumulated in longer bouts and sedentary behaviour accumulated in shorter bouts. In addition to the adverse effects of spending too much time sedentary, the assessment of patterns of activity behaviour also have implications for adverse health effects. A prospective study carried out between 2010 and 2011 among 430 older Japanese workers between the ages of 40–64 years showed that prolonged uninterrupted periods of sedentary behaviour independent of MVPA was associated with an increased risk of metabolic syndrome (Honda et al., 2016).

When looking at activity over a day, the knee OA participants were significantly more sedentary in the later hours of the day compared to the early hours of the day representing an hour by hour variation in SB, but the correlation was a weak one. The hourly variation of light physical activity showed that the knee OA patients in the present study were significantly more active in the mornings compared to the later parts of the day. This variation of activity may be attributed to pain in their knee or it could be because of the early morning stiffness which is usually relieved with movement. It could also be since it is dark outside making it unsafe to go out. Another reason could be that data collected during winter might show less activity than those collected during summer.

It is interesting to note that the patients were more active in the morning compared to the afternoon even when one of the criteria for diagnosis of knee OA is early morning stiffness. The early morning stiffness occurred around 6am (which was not different to the mean over day) after which (1 hour later from 7am) activity increased greater than the mean of the sample over the day. This activity was greater in the morning but only once the patients had got up and going (i.e. their morning stiffness had subsided. It is also important to note that the patients were relatively active compared to the

afternoon. Although we didn't compare these patients to a control group, these participants still only spent a maximum of approximately 23 minutes per hour in light physical activity in the morning, which compared to a healthy population is considered lower (WHO 2011). Furthermore these patients could have been engaged in self-care (e.g. washing, dressing, preparing for the day) in the early hours of the morning making them more lightly active.

Knowing what exactly is responsible for this variation in relation to activity behaviour in these patients, gives researchers justification for encouraging interventions at appropriate times of the day. Additionally, it will also be important to know what makes knee OA patients more sedentary in the later part of the day. Creating an intervention to improve their sedentary behaviour at these hours (i.e. maybe promote short walks) by replacing sedentary hours with light activities may prove to be vital in the management of knee OA populations. As mentioned earlier, emphasis on meeting the recommended MVPA per week in the older population especially one with a musculoskeletal disorder perhaps neglects the importance of regular light activity and reducing sedentary time. Bann and colleagues (2015) showed in a cross-sectional study comprising of community dwelling sedentary older adults (70-89 years of age) that substituting sedentary time with light intensity activity improves BMI and reduces the prevalence of obesity. Light physical activity also reduces the risk of sarcopenia (Aggio et al., 2016) and sarcopenia has been implicated in the prevalence of knee OA (Loeser, 2010). Therefore encouraging light physical activity in the elderly is important since it has been demonstrated that activity has an anti-inflammatory effect on joints and also known to increase muscle mass (Thomas et al., 2012).

Is objectively measured physical activity and sedentary behaviour associated with functional capacity/outcomes as assessed by self-report questionnaires?
The weak but significant correlations found between WOMAC (pain, ADL) with different patterns of activity contributes to previous knowledge on the relationship

between total activity behaviours and functional capacity (Huang et al., 2015). It also appeared that there were more significant associations between the WOMAC and activity and not the KOOS and activity. Perhaps because the KOOS has more subscales than the WOMAC (five versus 3) the relationships are diluted and therefore not many correlations are seen. The questions are similar and the questionnaires are lengthy and so perhaps the order in which they are completed presents a problem as the patients may not have fully cooperated in completing such lengthy questionnaires. The present study however showed that worse pain and activity of daily living scores (as measured using the WOMAC which is the most commonly used questionnaire in clinical assessments of knee OA) were associated with patients being more sedentary and having less favourable patterns of activity accumulation. Knee pain appears to be a major determining factor for physical activity and sedentary behaviour (Huang et al., 2015). However, there was also a relationship between a patient's ability to perform activities of daily living (WOMAC ADL) scores and their objectively measured patterns of activity. The use of accelerometers in these knee OA patients appeared to be useful in the clinical assessment of the functional ability of knee OA patients. The findings from my study are supported by findings from qualitative research on knee OA patients who have reported that they purposefully reduce their activity levels in order to relieve pain (Hawker et al., 2008). However, the causal relationship between pain and activity needs to be further explored. There however appeared to better correlation between the KOOS and WOMAC with the activPAL. This may be because the activPAL is better at measuring sedentary behaviour than is the ActiGraph (Steeves 2015). This is also substantiated by the stronger correlations seen between SB and the WOMAC than between MVPA and the WOMAC so it may be that the activPAL is better and more useful in this population of very sedentary adults.

Limitations and strengths of the study

To further this work, it would be helpful to include a control group to compare the data to a healthy age and gender matched population. This study was a cross sectional design therefore a causal relationship between pain and activity cannot be established. Also, it should be noted that influence of medication use (or not) might result in data being skewed. Therefore comparisons between patients who are on pain medication and those who are off medication should be made in future studies. However, a strength of the study is that I used two activity monitors. These monitors measured different aspects of physical activity and sedentary behaviour and therefore the detailed data that was obtained gave a clearer picture of the patterns of activity behaviours in this population. The assessment of the patterns of PA and SB, which for the first of its kind in knee OA population in South Africa, is also due to the use of two monitors in this sample of patients. Further studies should consider the reasons for the variation in daily activity and these reasons could possibly provide realistic intervention opportunities for these patients based on their daily habitual activities. The knee OA characteristics are in line with the aetiology of patients with knee OA in South Africa and the grade of severity of knee OA was the same in our participants.

CHAPTER 6: CONCLUSION

My study is the first to look at objectively measured patterns of PA and SB in knee OA patients in South Africa. From our findings we discovered that pain is the main factor responsible for a lower PA and also implicated in high SB, we also deduced that SB is mostly accumulated in bouts of greater than 30 minutes and light activity are mostly in bouts of less than five minutes. Another important finding is that our participants are more sedentary in the later part of the day. Therefore, it will be very beneficial to these populations if an intervention can be put in place to shorten these long sedentary bouts or to increase the short bouts of light PA. It is also important to shift attention from meeting recommendation of MVPA to creating a feasible outline of doing more light activity and breaking more sedentary time in knee OA population. Since the older healthy population is not meeting the recommended PA guidelines it is rather unrealistic to enforce this on a population with a musculoskeletal disorder.

Future research

Future studies should include an age matched control group so that patterns of PA and SB can be compared between the knee OA group and the controls. It will also be beneficial to include an objective measure of physical function (e.g. 6 minute walk test, chair standing) so that physical function can be compared with objectively measured patterns of PA and SB, and also with pain and function assessed subjectively.

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APPENDICES





GENERAL HEALTH QUESTIONNAIRE

We would like to know about your health. Please answer the questions below as accurately as possible. This questionnaire may be filled out electronically or you can fill it out by hand. If you fill it in electronically, to tick a box, double click the box and under default value select the checked option. Click ok. If you need to type, click in the box provided and write as much as is needed.
Thank you very much.

1) Compared to other adults your age, how would you rate your health in the last TWO years? Please tick one box.

Better than others	☐	Worse than others	☐
Same as others	☐	Much worse than others	☐

*2) **In the last TWO years:***

a) Have you gone to hospital? Yes ☐ No ☐

*b) If **yes**, what did you go to hospital for?*

c) How long did you stay in hospital for?

d) Have you had any surgical procedures in the last year? Yes ☐ No ☐

If yes, which procedure did you have?

3) Please tick any illnesses that you may have currently or have had in the last SIX months.

Illness		**How long ago?**	**Fully recovered?**
Heart attack, stroke	☐	_____	Yes ☐ No ☐
Diabetes Mellitus Type I	☐	_____	Yes ☐ No ☐
Diabetes Mellitus Type II	☐	_____	Yes ☐ No ☐
Cold	☐	_____	Yes ☐ No ☐
Influenza ('Flu)	☐	_____	Yes ☐ No ☐
High total cholesterol	☐	_____	Yes ☐ No ☐
None	☐		

4) Please write down any medication/treatment that you may be on or have taken in the last SIX months.

5) Do you smoke?

Yes ☐ No ☐

6) Please tick the box of the items that you own:

☐ Microwave	☐ Telephone – Landline	☐ Cell phone
☐ DSTV, Top TV	☐ Car How many?	☐ Formal housing
☐ Washing machine	☐ Fridge	☐ Indoor toilet
☐ Indoor water	☐ Video machine/DVD player	☐ Television
☐ Electricity	☐ Dishwasher	☐ Computer

☐ How many adults (over 18) in your family?

Highest level of education?

_____

THANK YOU FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE

WOMAC Osteoarthritis Index LK3.1 (IK)

INSTRUCTIONS TO PATIENTS

In Sections A, B, and C questions are asked in the following format. Please mark your answers by putting an " ✗ " in one of the boxes.

EXAMPLES:

1. If you put your " ✗ " in the box on the far left as shown below,

none	mild	moderate	severe	extreme
☒	☐	☐	☐	☐

then you are indicating that you feel **no** pain.

2. If you put your " ✗ " in the box on the far right as shown below,

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☒

then you are indicating that you feel **extreme** pain.

3. Please note:
   a) that the further to the right you place your " ✗ ", the **more** pain you feel.
   b) that the further to the left you place your " ✗ ", the **less** pain you feel.
   c) **please do not** place your " ✗ " **outside any of the boxes**.

You will be asked to indicate on this type of scale the amount of pain, stiffness or disability you have felt during the last 48 hours.

Think about your knee to be injected when answering the questions. Indicate the severity of your pain and stiffness and the difficulty you have in doing daily activities that you feel are caused by the arthritis in your knee to be injected.

Your knee to be injected has been identified for you by your health care professional. If you are unsure which knee is to be injected, please ask before completing the questionnaire.

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V3 - English for USA
(at baseline)

WOMAC Osteoarthritis Index LK3.1 (IK)

Section A

PAIN

Think about the pain you felt during the last 48 hours caused by the arthritis in your knee to be injected.

(Please mark your answers with an " ✗ ".)

QUESTION: **How much pain have you had . . .**					Study Coordinator Use Only
1. when walking on a flat surface?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PAIN1 ____
2. when going up or down stairs?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PAIN2 ____
3. at night while in bed? (that is - pain that disturbs your sleep)					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PAIN3 ____
4. while sitting or lying down?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PAIN4 ____
5. while standing?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PAIN5 ____

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Section B

STIFFNESS

Think about the stiffness (not pain) you felt during the last 48 hours caused by the arthritis in your knee to be injected.

Stiffness is a sensation of **decreased** ease in moving your joint.

(Please mark your answers with an " ✗ ".)

	Study Coordinator Use Only
6. How **severe** has your stiffness been **after you first woke up** in the morning? none ❑ mild ❑ moderate ❑ severe ❑ extreme ❑	STIFF6 ____
7. How **severe** has your stiffness been after sitting or lying down or while resting **later in the day**? none ❑ mild ❑ moderate ❑ severe ❑ extreme ❑	STIFF7 ____

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WOMAC Osteoarthritis Index LK3.1 (IK)

Section C

DIFFICULTY PERFORMING DAILY ACTIVITIES

Think about the difficulty you had in doing the following daily physical activities during the last 48 hours caused by the arthritis in your knee to be injected. By this we mean **your ability to move around and take care of yourself**.

(Please mark your answers with an " ✗ ".)

QUESTION: **How much difficulty have you had . . .**					Study Coordinator Use Only
8. when going down the stairs?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN8 ____
9. when going up the stairs?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN9 ____
10. when getting up from a sitting position?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN10 ____
11. while standing?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN11 ____
12. when bending to the floor?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN12 ____
13. when walking on a flat surface?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN13 ____

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WOMAC Osteoarthritis Index LK3.1 (IK)

DIFFICULTY PERFORMING DAILY ACTIVITIES

Think about the difficulty you had in doing the following daily physical activities during the last 48 hours caused by the arthritis in your knee to be injected. By this we mean **your ability to move around and take care of yourself**.

(Please mark your answers with an " ✗ ".)

QUESTION: **How much difficulty have you had . . .**					Study Coordinator Use Only
14. getting in or out of a car, or getting on or off a bus?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN14 ____
15. while going shopping?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN15 ____
16. when putting on your socks or panty hose or stockings?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN16 ____
17. when getting out of bed?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN17 ____
18. when taking off your socks or panty hose or stockings?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN18 ____
19. while lying in bed?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN19 ____

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WOMAC Osteoarthritis Index LK3.1 (IK)

DIFFICULTY PERFORMING DAILY ACTIVITIES

Think about the difficulty you had in doing the following daily physical activities during the last 48 hours caused by the arthritis in your knee to be injected. By this we mean **your ability to move around and take care of yourself**.

(Please mark your answers with an " ✗ ".)

QUESTION: **How much difficulty have you had . . .**					Study Coordinator Use Only
20. when getting in or out of the bathtub?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN20 _____
21. while sitting?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN21 _____
22. when getting on or off the toilet?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN22 _____
23. while doing heavy household chores?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN23 _____
24. while doing light household chores?					
none ❑	mild ❑	moderate ❑	severe ❑	extreme ❑	PFTN24 _____

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Knee injury and Osteoarthritis Outcome Score (KOOS), English version LK1.0

KOOS KNEE SURVEY

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

Name: _____

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

Symptoms

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

S1. Do you have swelling in your knee?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S2. Do you feel grinding, hear clicking or any other type of noise when your knee moves?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S3. Does your knee catch or hang up when moving?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S4. Can you straighten your knee fully?

Always	Often	Sometimes	Rarely	Never
☐	☐	☐	☐	☐

S5. Can you bend your knee fully?

Always	Often	Sometimes	Rarely	Never
☐	☐	☐	☐	☐

Stiffness

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

S6. How severe is your knee joint stiffness after first wakening in the morning?

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

S7. How severe is your knee stiffness after sitting, lying or resting **later in the day**?

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Pain

P1. How often do you experience knee pain?

Never	Monthly	Weekly	Daily	Always
☐	☐	☐	☐	☐

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

P2. Twisting/pivoting on your knee

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P3. Straightening knee fully

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P4. Bending knee fully

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P5. Walking on flat surface

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P6. Going up or down stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P7. At night while in bed

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P8. Sitting or lying

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P9. Standing upright

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Function, daily living

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

A1. Descending stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A2. Ascending stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A3. Rising from sitting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A4. Standing

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A5. Bending to floor/pick up an object

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A6. Walking on flat surface

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A7. Getting in/out of car

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A8. Going shopping

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A9. Putting on socks/stockings

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A10. Rising from bed

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A11. Taking off socks/stockings

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A12. Lying in bed (turning over, maintaining knee position)

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A13. Getting in/out of bath

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A14. Sitting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A15. Getting on/off toilet

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

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

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

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

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Function, sports and recreational activities

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

SP1. Squatting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP2. Running

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP3. Jumping

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP4. Twisting/pivoting on your injured knee

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP5. Kneeling

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Quality of Life

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

Never	Monthly	Weekly	Daily	Constantly
☐	☐	☐	☐	☐

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

Not at all	Mildly	Moderately	Severely	Totally
☐	☐	☐	☐	☐

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

Not at all	Mildly	Moderately	Severely	Extremely
☐	☐	☐	☐	☐

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

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Thank you very much for completing all the questions in this questionnaire.

APPENDIX D

UCLA Activity Score	Hip ID:
	Study Hip: ☐ Left ☐ Right
	Examination Date (MM/DD/YY): / /
	Subject Initials: |____|____|____|
	Medical Record Number:

Interval: _____

Check one box that best describes current activity level.

☐ 1: Wholly Inactive, dependent on others, and can not leave residence

☐ 2: Mostly Inactive or restricted to minimum activities of daily living

☐ 3: Sometimes participates in mild activities, such as walking, limited housework and limited shopping

☐ 4: Regularly Participates in mild activities

☐ 5: Sometimes participates in moderate activities such as swimming or could do unlimited housework or shopping

☐ 6: Regularly participates in moderate activities

☐ 7: Regularly participates in active events such as bicycling

☐ 8: Regularly participates in active events, such as golf or bowling

☐ 9: Sometimes participates in impact sports such as jogging, tennis, skiing, acrobatics, ballet, heavy labor or backpacking

☐ 10: Regularly participates in impact sports

MORNING FORM

Subject code: ……. Date: ……

1. What time did you go to bed last night? …….. : ……
2. What time did you turn out the light to go to sleep? …….. : ……
3. What time did you wake up this morning? ……. : ……...

Did you have to take any medication for your pain last night? If so,

What did you take?

……

What dosage?

……

At what time?

…….

COMMENTS:

Please make a note on whether you were disturbed during the night, were uncomfortable, or whether there was anything unusual about your sleep.

……

……

……

……

SEVERITY OF PAIN

Please make a mark on the line to indicate the degree of knee osteoarthritis associated pain you feel this morning.

On the body chart below please indicate where you experienced pain last night.

No pain at
all

Worst pain

I have

ever felt

R14/49 Dr Rebecca Meiring and Prof Dick an der Jagt

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M150323

NAME: (Principal Investigator)	Dr Rebecca Meiring and Prof Dick an der Jagt
DEPARTMENT:	Orthopaedics Exercise Physiology Laboratory, School of Physiology Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	The Effect of Unilateral Knee Arthroplasty on Objectively Measured Physical Activity and Sedentary Behaviour Outcomes
DATE CONSIDERED:	27/03/2015
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	08/07/2015

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

R14/49 Emmanuel Frimpong and Yusuf Kaoje et al

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M170297

NAME: (Principal Investigator)	Emmanuel Frimpong and Yusuf Kaoje et al
DEPARTMENT:	Physiology School of Physiology Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	The Effect of Unilateral Knee Arthroplasty on Objectively Measured Physical Activity and Sedentary Behaviour Outcomes
DATE CONSIDERED:	Adhoc
DECISION:	Approved unconditionally
CONDITIONS:	Sub-Study (M150323)
SUPERVISOR:	Dr Rebecca Meiring
APPROVED BY:	Professor P. Cleaton-Jones,Chairperson, HREC (Medical)
DATE OF APPROVAL:	13/03/2017

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004,10th floor, Senate House/2nd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. I/We fully understand the the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially review in February and will therefore be due in the month of February each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES