THE EFFECTS OF TOTAL KNEE ARTHROPLASTY ON HABITUAL PHYSICAL ACTIVITY, SEDENTARY BEHAVIOUR AND HEALTH OUTCOMES IN OSTEOARTHRITIS PATIENTS

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DECLARATION

I, Emmanuel Frimpong, declare that this Thesis is my own, unaided work. It is being submitted for the Degree of Doctor of Philosophy at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

Signed

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This 11th day of June 2018 in Johannesburg

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PREFACE

The studies presented in this thesis are novel research reports on activity behaviours of patients with knee osteoarthritis (OA) in South Africa and the general knee OA population. Prior to this study, physical activity (PA) levels and sedentary behaviour (SB) of patients with knee OA from low to middle income countries (such as South Africa) undergoing a primary total knee arthroplasty (TKA) had not been studied. Previous studies objectively measuring PA and/or SB had only originated in high-income countries and have generated conflicting and inconsistent findings regarding improvements in these activity behaviours following the surgery. Whereas some studies reported improvement in PA and/or SB, others observed no improvements following TKA. In addition, the detailed patterns by which patients with knee OA accumulate PA and SB before and after TKA have not been studied. Most studies have reported significant improvements in health outcomes measured subjectively by patient-reported outcome measures (PROMs), but the results for objectively measured outcomes have been inconsistent. Consequently, the associations between objectively measured PA and SB and health outcomes (such as pain, physical function and quality of life) are unclear. Furthermore, the SB of patients with knee OA before and after TKA has received far less attention (than has been paid to PA) and has been superficially described in the very few studies that have reported some aspects of SB. Indeed, a thorough review of the literature revealed that there was no systematic review integrating available evidence on changes in SB following TKA, necessitating a study in this regard. Subsequently, it was imperative to conduct an observational longitudinal study using accelerometers (ActiGraph GT3X+ and ActivPAL) to objectively analyse volume and patterns of PA and SB before and after a primary TKA. Furthermore, there was a need to also study the associations between changes in objectively measured PA, particularly activities at low intensities (which occur in daily routines and a promising area of PA research), and the changes in self-perceived physical function of patients following TKA.

This thesis has been organized and written up into six chapters. Chapter 1 is a review of literature presented as an overview of what is known and gaps in knowledge on PA and SB in patients with knee OA before and after TKA. Chapter 2 presents a systematic review on changes in SB following TKA (as study one of this thesis). Chapter 3 details the methods used in the longitudinal study (Study 2A and B). Chapter 4 presents the results of the longitudinal study (Study 2A and B). Chapter

5 presents the discussion of the findings of the longitudinal study (Study 2A and B). Finally, chapter 6 presents the summary of the main conclusions of the thesis as a whole.

The work presented in this thesis is based on the following publications and presentations that have emanated from data collected for the thesis.

Peer Reviewed Publications:

Meiring RM, Frimpong E, Mokete L, Jurek P, Dick VDJ, Tikly M and McVeigh JA. Rationale, design and protocol of a longitudinal study assessing the effect of total knee arthroplasty on habitual physical activity and sedentary behaviour in adults with osteoarthritis. *BMC Musculoskeletal Disorders*. *2016,17: 281* (Appendix J).

Frimpong E, McVeigh JA, Meiring RM.. Sedentary Behaviour in Patients with Knee Osteoarthritis before and after Total Knee Arthroplasty: A Systematic Review. *J Aging Phys Act. 2017, 18:1-38.doi: 10.1123/japa.2017-0214 (Abstract of the accepted version inserted in appendix K).*

Frimpong E, McVeigh JA, van der Jagt D, Mokete L, Kaoje YS, Tikly M, Meiring RM. Light intensity physical activity increases and sedentary behaviour decreases following total knee arthroplasty in patients with osteoarthritis. *Knee Surg Sports Traumatol Arthrosc (2018). https://doi.org/10.1007/s00167-018-4987-2 (Appendix L).*

Frimpong E, van der Jagt Dick, Mokete L, Kaoje YS, Tikly M, McVeigh JA, Meiring RM. Objectively measured changes in changes in times spent sitting, standing and walking and their association with health outcomes of patients with knee osteoarthritis undergoing total knee arthroplasty. *In preparation to be submitted to BMC Musculoskeletal Disorders*

Meiring RM, Frimpong E, Mthembu NH, Kaoje YS, van der Jagt D, Tikly M, McVeigh JA. A Comparison of Objectively Measured Physical Activity and Sedentary Behaviour between Patients with Knee Osteoarthritis and Rheumatoid Arthritis. *In preparation to be submitted to Arthritis Care and Research.*

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ABSTRACT

Knee osteoarthritis (OA) is the most prevalent form of OA and it is present in over 33% of adults aged 50 years and above. Patients with end-stage knee OA have poor health outcomes including severe knee pain, functional limitations and poor quality of life (QoL) with decreased physical activity (PA) and increased sedentary behaviour (SB). In spite of the cost-effectiveness of total knee arthroplasty (TKA) in improving patients' health outcomes (as measured using patient-reported outcome measures (PROMs)), the objectively measured PA shows little or no change after surgery and SB has received very little attention following TKA. However, published studies have only been conducted in populations from high-income countries and no studies have assessed PA and SB in knee OA patients from low-middle income countries including South Africa. Furthermore, the detailed patterns by which patients with knee OA accumulate PA and SB before and after TKA have not been described. Studies have mainly focused on measuring overall PA or moderate to vigorous PA (MVPA) and/or patients' adherence to the PA guidelines with very little attention to low intensity activities of the movement continuum (SB and light activity- LPA). Furthermore, different activity monitors have been used with very few of them capable of measuring low intensity activities. Assessing activity behaviours incidental in activities of daily living (ADL) (such as sitting, standing and walking) before and after TKA may be clinically useful as activities of older adults undergoing TKA mainly constitute these low intensity activities.

With no previously published systematic review on changes in SB following TKA, the objective of the first study of this thesis was to integrate available evidence on changes in SB in patients with knee OA after a primary TKA. A systematic literature search from January 2002 to 31 October 2017 was performed across seven electronic databases, for longitudinal and cross-sectional studies published in English on objectively (through accelerometry) and/or subjectively measured changes in SB following TKA. Ten studies reporting on SB with a total of 1,028 participants were included in the review. Three studies reported changes in SB with two showing a reduction in SB and one, with high risk of bias, showing an increase in SB after TKA. Seven studies showed no change in SB following TKA.

The second study of this thesis was a longitudinal design comprising of two parts (Study 2A and B). Participants wore two activity monitors (ActiGraph GT3X+ and

ActivPAL) to measure PA and SB for seven consecutive days (24 hours/day) at baseline (preoperative), six weeks and six months after TKA. Therefore, the second objective (Study 2A) of this thesis was to objectively measure changes in volume and pattern of PA and SB (using ActiGraph GT3X+ accelerometer) in patients with knee OA from baseline to six months after TKA and to assess changes in PROMs following TKA. Eighty-nine patients (13 males, 76 females between 55 and 80 years of age) scheduled for primary TKA took part in the study. Physical activity and SB were measured with an ActiGraph GT3X+ accelerometer for seven consecutive days (24 hours/day) and range of motion (ROM) was measured prior to TKA, and six weeks and six months after TKA. The University of California Los Angeles (UCLA) Activity index and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) were used to assess self-reported activity and physical function respectively. Of the initial 89 patients recruited, 57 completed the six months follow-up and 45 had valid activity data at the 6 months follow-up. The proportion of time (% of waking day) patients spent in light physical activity (LPA) increased from baseline [29.0 (26.6-31.4)%] to 6 months [34.8 (31.3-38.3)%; p=0.008]. However, time spent in moderate to vigorous PA (MVPA) did not change from baseline [median (interquartile range): 2.0 (7.8) min/day] to six months after TKA [3.4 (11.6) min/day, p>0.05]. Approximately 9%, 5% and 18% of the patients met the PA guidelines at baseline, and six weeks and six months after TKA respectively. The proportion of time (% of waking day) patients spent in SB decreased after TKA [baseline: mean (95% CI): 70.1 (67.5-72.7)%; six months: 64.0 (60.6-67.9)%; p=0.009]. The interruptions to SB increased between baseline and six months after TKA [mean (95% CI): 85.0 (80.0-90.0) to 93.0 (88.0-98.0) breaks/day, p=0.014]. There was a significant improvement in WOMAC score [median (interquartile range): 71.0 (27.0) vs. 4.0 (11.3), p<0.001], UCLA score [median (interquartile range): 2.0 (1.0) vs. 5.0 (1.0), p<0.001] as well as ROM [mean range: (0.0 - 90.0)° vs (0.0 - 110)°, p<0.05] between baseline and six months after TKA.

Study 2A showed that LPA increased and SB decreased as measured using ActiGraph GT3X+. In addition, self-reported functional capacity (FC) or functional ability (as measured with PROMs) improved after TKA. The third objective (Study 2B) of this thesis was to objectively assess changes in the times spent sitting, standing and walking following TKA and to examine their associations with the changes in PROMs after TKA. The same patients in Study 2A also wore a second activity monitor, the ActivPAL (which accurately measures low intensity activities and posture) for the same periods of time as described in Study 2A above. Patients spent significantly more of their waking wear time walking at six months after TKA (mean% (95% CI): 10.8% (9.4-12.1)), than preoperatively (mean% (95% CI): 8.3% (7.7-10.0)), p=0.039), however, the percentage of daily time spent standing did not change at six months after TKA (mean% (95% CI): 34.2% (29.8-38.6)) compared to percentage time preoperatively (mean% (95% CI): 32.4% (28.6-35.5)), p=0.530). Patients decreased their average daily time spent sitting from preoperative to six months after TKA by 33.7 mins/day (95% CI: -18.9 – 106.3, p=0.099). Patients took significantly more steps per day at six months after TKA [mean (95% CI: 3670 (2886-4020)] steps/day compared to preoperatively 2570 (2366-3189) steps/day, p<0.001. Participants also increased their cadence (steps/min) six months after surgery [mean (95% CI): 33 (31-34) vs. 38 (33-39), p=0.004]. There were no associations between objectively measured changes in the time spent sitting, standing and walking and changes in PROMs (p>0.05).

The studies presented in this thesis have novel aspects that extend the body of knowledge on activity behaviours of patients with knee OA undergoing TKA. The studies in this thesis report the first systematic review on changes in SB of knee OA patients following TKA. This thesis is the first to objectively measure the detailed patterns of PA and SB in patients with knee OA undergoing TKA from a low-middle income country (South Africa). Furthermore, this thesis is also the first to use two accelerometers to generate detailed activity behaviour in patients with knee OA undergoing TKA. Lastly, this thesis is the first to assess the association between changes in times spent sitting, standing and walking in relation to changes in health outcomes in knee OA patients after TKA.

In conclusion, the systematic review showed that SB has been superficially described and there is insufficient evidence to suggest that time spent in SB decreases following TKA. Majority of the studies reported no change in SB after TKA. The longitudinal study showed that, following TKA, there was a decrease in the overall time spent in SB and an increase in the number of breaks in SB that appeared to be replaced by LPA. Participants' volume and average daily cadence increased following TKA. In addition, participants decreased their time spent sitting by over half an hour at six months after TKA. However, there were no associations between changes in the times spent sitting, standing and walking and changes in measures of participants' health outcomes (PROMs) following TKA. Both objective and subjective measures should be used to accurately assess improvements in patients' health outcomes following TKA. This comprehensive analysis of detailed daily activity behaviours can be used to employ feasible interventions for increasing the duration of LPA (standing and walking) and decreasing sedentary time (sitting/lying) to improve quality of life and overall health following TKA.

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ACRONYMS AND ABBREVIATIONS

ACL	Anterior cruciate ligament
ADL	Activities of daily living
BMI	Body mass index
COX-2	Cyclooxygenase-2
cpm	Counts per minute
COPD	Chronic obstructive pulmonary disease
DM	Diabetes mellitus
EE	Energy expenditure
FC	Functional capacity
IDEEA	Intelligent device for energy expenditure and activity
KOOS	Knee Injury and Osteoarthritis Outcome score
LHS	Length of hospital stay
LPA	Light physical activity: physical activities resulting in energy expenditure of 1.6 – 2.9 METs.
METs	Metabolic equivalents
MVPA	Moderate and vigorous physical activity: physical activities expending energy of ≥3 METs
NHANES	National Health and Nutrition Examination Survey
NEAT	Non-exercise energy thermogenesis
NSAIDs	Non-steroidal anti-inflammatory drugs
OA	Osteoarthritis
OAI	Osteoarthritis Initiative
OARSI	Osteoarthritis Research Society International
OKS	Oxford Knee Score
PA	Physical activity
PAEE	Physical activity energy expenditure
PROMs	Patient-reported outcome measures
QoL	Quality of life
ROM	Range of motion
SES	Socioeconomic status
SB	Sedentary behaviour
THA	Total hip arthroplasty

TKA	Total knee arthroplasty
UCLA	University of California Los Angeles Activity index
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

CHAPTER 1 – LITERATURE REVIEW

1.1 Introduction

Osteoarthritis (OA) is a progressive degenerative disease characterised by pain and disability due to joint failure (1–3). The joint failure is as a result of an imbalance between the breakdown and repair of joint tissues (1). Osteoarthritis has been described as an increasing major musculoskeletal problem and cause of disability (4). About 50% of older adults above the age of 65 years have OA (5). It was estimated that 27 million US adults had OA based on symptoms and physical findings (6). In South Africa, OA was reported to be the most common arthritic disease with a prevalence of 55.1% of adults aged 65 years and older (7). It has been projected that about half of all adults may develop symptomatic OA in their lifetime and the incidence may increase with increasing age (8,9) and obesity (10).

Osteoarthritis of the knee is the most prevalent form of OA (11) and symptomatic radiographic knee OA is present in 33% of adults aged 50 years and above (12). Patients with symptomatic knee OA have poor health outcomes including, severe knee pain, functional limitations and poor quality of life (13–15). In addition, patients with knee OA experience fatigue (10) and about 80% of the patients have movement disabilities (16) with decreased physical activity (PA) (17) and increased sedentary behaviour (SB) (18). Being physically inactive and highly sedentary can lead to sarcopenia in older adults (19), elevated blood pressure, weight gain and loss of functional ability in patients with knee OA (18,20–22). Loss of physical functional ability results in functional dependence in the community (23), increased medical costs (24,25), depression, obesity and poor knee confidence (26).

The most successful and cost-effective treatment for end-stage symptomatic knee OA is total knee arthroplasty (TKA) (27,28). Total knee arthroplasty is performed with the aim of improving pain, functional performance and quality of life (29,30). The demand for TKA is rising steeply and knee OA accounts for 94-97% of all TKAs performed (31). In the UK, the National Joint Registry reported that a total of 103,126 TKAs were done between 2015 and 2016 (32). In South Africa, the 2016 South African National Joint Registry (SANJR) Annual Report showed that, between December 2012 and December 2016, of the total number (3,961) of primary TKAs done, 95.4% were due to knee OA (33).

Historically, assessment of health outcomes following TKA has been done subjectively with patient-reported outcome measures (PROMs). For example, knee OA-specific PROMs such as the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index, Knee injury and Osteoarthritis Outcome Score (KOOS) and Oxford Knee Score (OKS) as well as the activity rating tool such as the University of California Los Angeles (UCLA) Activity index, have been effectively used to enable patients to report changes in health outcomes following TKA (34–36). Studies using these PROMs have reported improvements in pain, physical function, ability to perform daily routines, quality of life (29,35,37–42) and self-reported PA (43–47). The PROMs like other self-report measures are easy to administer, readily accessible and inexpensive, but they have poor validity and reliability and are biased regarding recall (35,48,49). The inherent limitations of self-reported instruments for assessing activity behaviours (SB and PA) and health outcomes have necessitated the development and use of more objective methods (including wearable activity monitors) to assess functional ability (50,51). The advent of wearable PA monitors (such as accelerometers) to objectively assess combinations of activity behaviours has enabled better study of the important associations between activity and health outcomes (52).

Studies that have used accelerometers for the assessment of PA after TKA (39,40,42,53) have often reported no or very little change in PA compared to those studies that have reported improvements in PROMs and self-reported PA (43–47). Moreover, recent systematic reviews with and/or without meta-analyses have shown that actual PA at six months postoperatively does not change, but a small improvement occurs at 12 months postoperatively (54,55), but conclusions have been based on the very few available studies. Furthermore, studies have yielded conflicting findings on overall SB changes following TKA (40,42,53) and the only available systematic review concluded that there is insufficient evidence to show that SB change following TKA (56). However, previous studies have measured activity behaviours (PA and SB) between different preoperative and postoperative patient populations (57–59), and monitored activity over shorter number of days (39,42,60) than the three to seven days recommended for adults (61). Some studies were underpowered (40,62), while in other studies, activity was measured at only one time point postoperatively (40,63,64). The detailed patterns by which patients with knee OA accumulate PA and SB before and after TKA have not been described. In addition, previous studies have originated in high-income countries with only one study recently published from a low-middle income country that demonstrated an increase in light physical activity (LPA) and a decrease in SB following TKA for a symptomatic end-stage knee OA (65).

The focus of PA assessments pre- and postoperatively have mainly centred on measuring overall PA and/or determining the proportion of patients who comply with the PA guidelines of 150 min of moderate and vigorous physical activity (MVPA) per week (66). However, less than 50% of symptomatic knee OA patients comply with the PA guidelines postoperatively (40,45,57,58,64,67,68). The increased attention for measuring MVPA following TKA has in part, resulted in the neglect of activities at the lower end of the movement continuum (SB and LPA) (69,70). Additionally, people tend to recall more accurately activities of moderate and higher intensities compared to those of lower intensity as large-scale epidemiological studies have been conducted with self-report questionnaires (71,72). Low intensity activities constitute most of the activities of the waking day, however they are not included in the PA guidelines and hence, no guidance is given for their accumulation throughout the day. Given that the majority of patients undergoing TKA are older adults whose activities in the waking day constitute mainly SB (such as sitting) and LPA (including standing and walking) (73), assessing these activity behaviours before and after TKA would be more useful clinically, especially when these activities are incidental in activities of daily living (ADL). Modification of lower intensity activities may be a more feasible target for post-operative rehabilitative interventions to alleviate the symptoms that may have accompanied or exacerbated the knee OA, e.g. obesity. Furthermore, the discordance between objectively measured PA and PROMs following TKA may suggest poor associations between the two constructs; however, this has as yet not been demonstrated.

Currently, there is no consistent detailed objective way of knowing whether functional capacity (FC), that is, ability to perform ADL, has improved postoperatively, especially in terms of whether lower intensity activity might change. Given that PA in knee OA patients varies from one country to another (74), it is important to ascertain whether knee OA patients in South Africa meet the daily recommended PA levels and their pattern of accumulation of objectively measured activity behaviours (PA and SB). Knowing the PA levels of South African knee OA patients undergoing TKA, would enable the development and implementation of specific clinical guidelines and informed targeted interventions for improving PA as well as overall health and quality of life of patients. Measuring total sedentary time, breaks in sedentary time, bouts of sedentary time and patterns of accumulation of sedentary time may be a better way of assessing SB change and its implication on health outcomes than measuring only total volume of SB before and after TKA.

The following sections of this chapter present the relevant review of literature on knee OA and more emphasis has been placed on PA and SB and their measurements in patients undergoing TKA, highlighting areas of gaps in knowledge.

1.2 Brief anatomy of the knee joint

The knee is the largest and most weight bearing as well as heavily loaded joint of the human body (75). It is a complex hinge joint that allows the greatest range of motion (ROM) in flexion, extension, limited rotation and gliding (76,77). During movement, the knee maintains stability and control (76). The joint consists of four articulating bones namely: femur (thigh bone), tibia (shin bone), patella (knee cap) and fibula (78). The bones at the knee form two articulations: the tibiofemoral and patellofemoral articulations (78). The patellofemoral articulation enables the knee to bear the body weight while articulation between femur and patella ensures smooth transmission of muscular forces over the knee (76,78). Thus, the knee is conceptualized as having three compartments: lateral tibiofemoral, medial tibiofemoral and patellofemoral compartments (79).

The articular ends of the femur (distal ends) and tibia (proximal end) are covered with cartilage, which allow smooth joint articulation and also help in lubricating the joint (80). There are also menisci (medial and lateral) between the articular cartilages of the femur and tibia that act as shock absorbers and cushion the joint for weight bearing or loading (78,81). The fluid-filled structures, bursae facilitate movement by reducing friction between tendons and adjacent structures (76). The joint has a capsule reinforced by the extra-articular ligaments and an internal synovial membrane that lines the articular surfaces of the joint and produces synovial fluids that lubricate the joint and provide nutrients in the joint (78). The knee joint is primarily supported and stabilized by the intra-articular and extra-articular ligaments (78,82) and muscles (with tendons) surrounding or crossing the joint further stabilize and support the knee joint as they primarily cause motions at the joint (76).

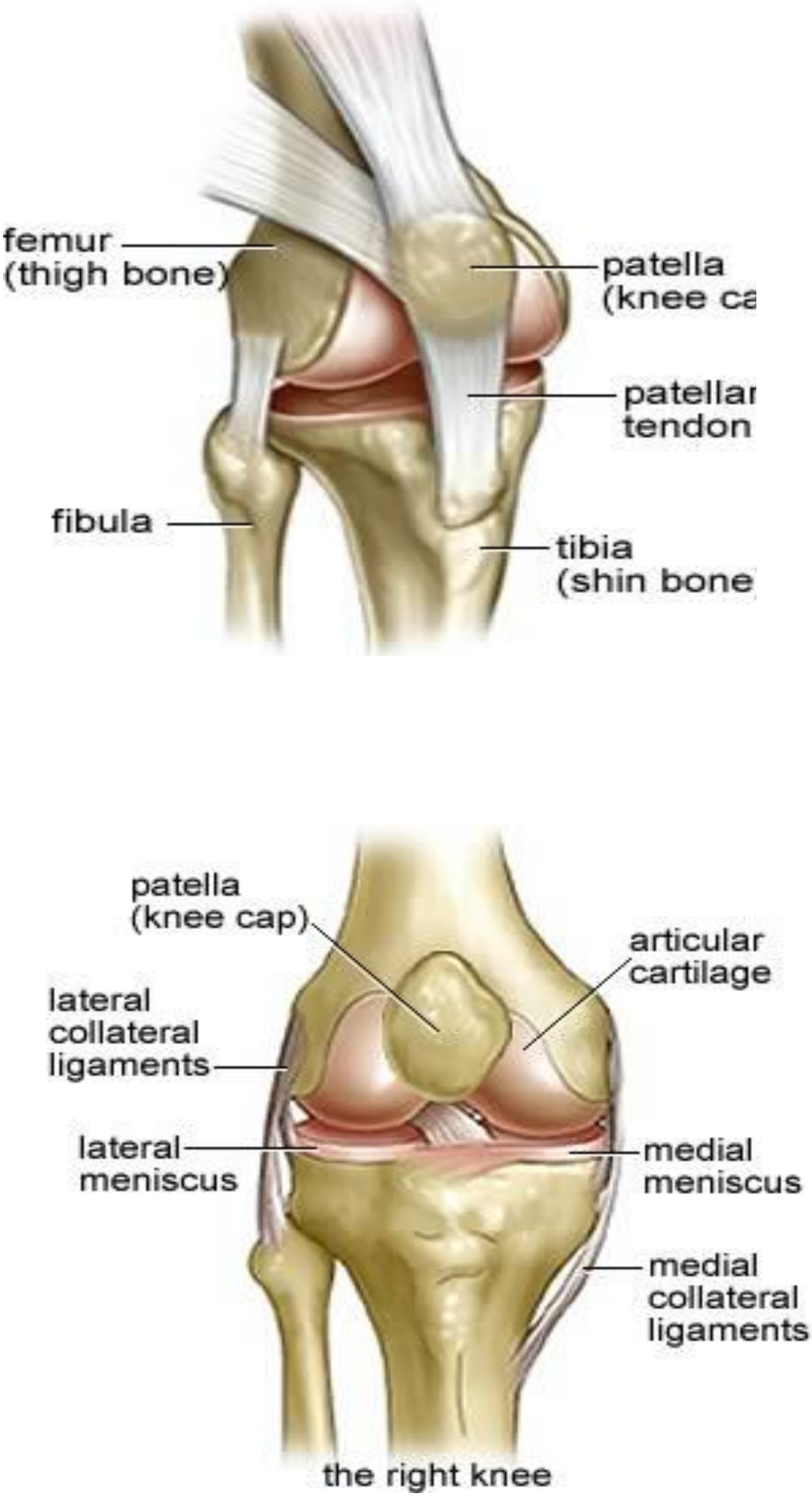

Figure 1. 1 Showing the structure of the knee joint taken from ACL Solutions (83).

1.3 Definition of osteoarthritis and overview

Osteoarthritis is a disease characterised by the degeneration of the articular cartilage that provides smooth joint movement (84). This degeneration results in matrix fibrillation, fissure appearance, gross ulceration and joint-space narrowing (84). Osteoarthritis is also known as the degenerative disease of the synovial joints (85). Depending on the underlying cause, OA may be classified as either primary or secondary (85). Primary OA is the most common form of OA and has no known cause but it is associated with ageing (85). However, secondary OA may have an identifiable underlying cause such as trauma or other disease process such as rheumatoid arthritis (85). Figure 1.2 shows a radiograph of a typical case of OA of the knee joint with the characteristic features (86).

Pathologically, OA adversely affects several structures of the knee joint such as the articular cartilage, synovial lining, periarticular bone and other connective tissues that support the joint (79,87). Generally, the structural changes in knee OA involve the progressive loss of articular cartilage, subchondral plate thickening, osteophyte formation (growth of new bones at joint margins), capsular thickening, periarticular muscle weakness and formation of subchondral cysts (79,88). The joint failure is due to imbalance between breakdown and repair of joint tissues (1).The loss of cartilage in a local area leads to further cartilage loss leading to a large area of cartilage loss or bony remodeling, which causes the tilting of joint and development of malalignment (79). The malalignment of the joint further increases local joint loading and hence, creating a vicious cycle of joint damage leading to joint failure (79). Figure 1.1 shows a normal knee joint.

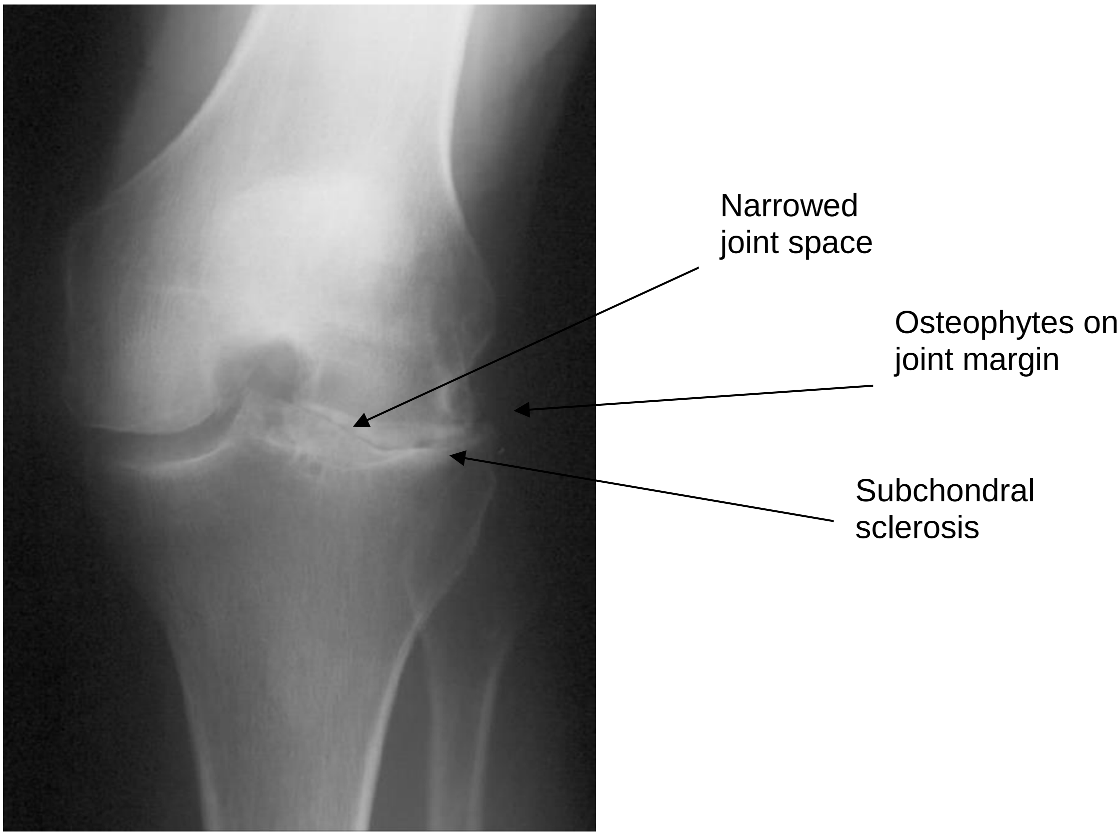

Figure 1. 2 A radiograph showing characteristic features of end-stage knee osteoarthritis

(86).

1.4 Epidemiology of osteoarthritis and knee osteoarthritis

Osteoarthritis is the most prevalent form of arthritis and the leading cause of disability in older adults (8,89). Globally, OA affects 40% of adults above the age of 70 years and affects more than 12% of adults in the US (18,90). The 2010 Global Disease Burden report revealed that the prevalence of knee OA was highest in the Asia Pacific high-income region, followed by Oceania and North Africa/Middle East but lowest in South and Southeast Asia (4,8). In 2015, a systematic review and meta-analysis showed that OA was the commonest arthritic disorder, with 55.1% and 30% of older adults in urban and rural South Africa respectively, having the disorder (7). Although the prevalence of OA varies depending on the geographical area, it increases steeply with age, with women having higher rates than men, particularly after 50 years of age (14). Osteoarthritis commonly affects stressed and weight-bearing joints such as those of the hands, spine, hips and knees (91). The knee is the most common joint affected in OA, with about 41% of limb arthritis found in the knee compared to 30% and 19% in the hands and hips respectively (11). Painful knee OA is present in about 50% of adults aged 50 years and over with radiographic evidence of OA (12).

Globally, as the population ages and with obesity reaching epidemic proportions, knee OA is more likely to become a major problem for health systems with demands for joint arthroplasty increasing significantly (4,8). Out of the 291 diseases covered in the Global Burden of Disease 2010 study, hip and knee OA were ranked the 11th highest contributor to global disability after diabetes and falls but were above drug use disorders and hearing loss (8). Furthermore, years lived with disability for knee OA increased from 10.5 million in 1990 to 17.1 million in 2010 (8). In addition, socioeconomic and ethnic factors are associated with knee OA (92). The prevalence of knee OA and the associated limitations in functional capacity or ability (ability to perform ADLs) are higher in people with low socioeconomic status compared to those with high socioeconomic status (93). Therefore, there is a need to increase research on patients with knee OA from low to middle income countries such as South Africa.

1.5 Risk factors of knee osteoarthritis

The cause of primary knee OA is unknown despite the high prevalence and morbidity (94). However, a number of risk factors may act to increase susceptibility to knee OA (14). Risk factors such as older age, female gender, obesity, previous knee injury, presence of hand OA as well as PA are consistently associated with an increased risk of knee OA (35,95,96). Physical activity may both be a risk factor and protective factor for the development and progression of knee OA depending on the type and intensity of PA (35). Physical activities with excessive or heavy, repetitive mechanical loading can induce degeneration of articular cartilage of the knee (35,96). Occupational activities involving kneeling, stooping or crouching are associated with knee OA (95). However, PA also protects against functional decline and improves functional independence in patients with knee OA (35,96). Furthermore, patients with knee OA can perform PA of moderate/high intensities that do not cause pain or predispose to injury (96).

The number of patients with knee OA is predicted to increase over the next decades with populations ageing in both developed and developing countries (8). The prevalence of knee OA increases indefinitely with age as the disease is irreversible (97). Epidemiological studies show that, the overall prevalence of knee OA is higher in females than in males and it tends to increase dramatically after menopause (98). However, the prevalence of knee OA is higher in males below 45 years of age compared to females, but females tend to be more affected after age 45 than males (97). Increased body weight or BMI precedes the occurrence of OA and is also associated with the disease progression (99). Approximately 25% of knee OA cases are significantly associated with obesity whereas only 5.1% are associated with previous injury to the knee joint (100). In another study, it was concluded that obesity is an important risk factor of knee OA and that modifying obesity may cause a significant reduction in the risk of knee OA in the general population (101). The Framingham Study found that a decrease in BMI of at least two units over the 10-year period decreased OA risk by 50% and concluded that weight loss reduces the risk for symptomatic knee OA in women (102). In South Africa, the National Panel Survey (2008-2012) revealed that the prevalence of obesity increased from 23.5% to 27.9% between 2008 and 2012 and it was more prevalent in females (37.9%) compared to males (13.3%) (103). The rising prevalence of obesity (103,104) with decreased PA (104) in South Africa raises concerns that the prevalence of knee OA and its co-morbidities will also steadily increase. It is most likely that the demand for treatment or need for management of knee OA will mirror the rising trend of obesity.

1.6 Clinical features of knee osteoarthritis and diagnosis

The clinical features of knee OA include chronic pain, stiffness or decreased range of motion (ROM), local inflammation with tenderness upon joint palpation, crepitus on motion, muscular weakness especially quadriceps, joint instability and alteration in proprioception (3,14,91). Radiographically, knee OA is evidenced by joint space narrowing, osteophytes, subchondral cysts and bony sclerosis (11). However, there is a discordance between radiographic changes and symptoms, where radiographical changes in the joint are not always associated with pain, stiffness and functional limitations, just as joint pain is also not always associated with radiographic abnormality (14,97). As result, the commonly used criterion to confirm radiographic knee OA is the Kellgren-Lawrence grades of 2-4 (97), where the characteristic features are scored (presence of osteophytes, joint space narrowing and sclerosis as shown in figure 1.2 above) (86). Clinically, symptomatic OA (which is the presence of pain and radiographic changes) is more important than knee pain or radiographic changes alone (86) as it is the symptomatic OA that causes suffering, disabilities and healthcare utilization (105). The signs and symptoms of knee OA are often associated with functional limitations (79). The disease causes limitations in physical functional ability including performance of activities of daily living (ADL), job and leisure pursuits (13,89,90,106). Osteoarthritis of the knee also results in poor quality of life (QoL) with co-morbidities such as sleep disturbances, depression, physical inactivity, obesity and polypharmacy with a significant economic impact (14,41,107).

The source of pain in knee OA is not well understood (86). The articular cartilage is an unlikely source of pain in knee OA given that the cartilage lacks nociceptive innervation (79). However, pain may originate in the patellofemoral compartment of the joint and bone and may also be due to synovial inflammation and as a result of distended capsule due to fluid accumulation (108,109). The nociception is initiated from free nerve endings located in the synovium, periosteal bone and tendons (110). In addition, it has been posited that, the interplay among biological, psychological and social factors may better explain pain in knee OA (110).

1.7 Treatment of knee osteoarthritis

The main goal of knee OA treatment is to improve health outcomes including pain relief, improving functional capacity and quality of life (29,30,111,112). Other goals of OA treatment may include improving habitual PA with a decrease in SB (111,30). The treatment for knee OA involves both surgical and non-surgical (pharmacological and non-pharmacological) approaches (113). The most commonly recommended medical treatment for knee OA is the non-surgical approach (11,113). However, knee OA may eventually necessitate the need for a surgical treatment (114).

1.7.1 Non-surgical or conservative treatment of knee OA

Several studies have been conducted to investigate the effectiveness of non-surgical interventions for patients with knee OA and/or awaiting surgery. The preoperative non-surgical interventions such as education and exercise programmes aim at improving preoperative outcomes as well as enhancing recovery postoperatively (115). Strengthening of muscles improve pain and joint stability (79,116). As a result, public health and clinical guidelines recommend some amount of exercise as an important intervention in the management of knee OA regardless of disease severity (117,118). The OA Research Society International (OARSI) guidelines recommend land- and water-based exercises, strength training, weight and self-management and education as the core non-surgical treatments appropriate for all patients with knee OA (117). Specifically, low-impact aerobic exercises are found to be effective and hence, recommended for improving pain, physical function and QoL in patients with knee OA (118,119). Furthermore, task-oriented activities or ADLs are beneficial for patients with knee OA (79).

Weight reduction is an important goal in the management of knee OA (117) and significant weight loss has positive effects on knee OA outcomes. One study revealed that, achieving weight loss of 5.1% or at rate of >0.24% weight reduction per week significantly improved physical disability and pain (120). A randomized trial comprising exercise and weight loss, weight loss alone and education showed that exercise and weight loss (but not weight loss alone) significantly improved pain and physical functions in knee OA patients compared with educating patients on nutrition, exercise and arthritis (121).

Pharmacological treatments are normally administered to knee OA patients with or without co-morbidities (such as diabetes, hypertension, cardiovascular diseases, renal failure, gastrointestinal bleeding, depression as well as physical impairments limiting activity including obesity) (117). Studies have shown that non-steroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase-2 (COX-2) inhibitors have higher efficacy compared to acetaminophen (paracetamol) (122,123). Other pharmacological treatments include hyaluronic acid injection, corticosteroid injection, glucosamine and chondroitin sulphate supplements (79).

1.7.2 Surgical treatment of knee osteoarthritis: Total knee arthroplasty (TKA)

Total knee arthroplasty (TKA) is a surgical treatment for end-stage knee OA that involves replacement of the damaged joint surfaces by an artificial joint or a knee implant (Figure 1.3) (85). In TKA, the articular ends of distal femur and proximal tibia are replaced with metal ends and an insert placed between them (85). The TKA was first introduced in 1973 (by Insall and colleagues) as a "total condylar knee prosthesis" and was described as a non-hinged surface replacement for almost all knee deformities (124). The total condylar prosthesis was developed as a result of some disadvantages (such as tibial component sinking and loosening and residual pain from unsurfaced patellofemal compartment) of the previously used ones (the duocondylar, geometric and Freeman-Swanson) (125). For the past four decades, several implants have been designed and used with varying cost-effectiveness (126). Currently, TKA is the most definitive and cost-effective surgical treatment for end-stage knee OA after all conservative treatment measures have been exhausted, and usually if pain persists for at least six months (27,28,37). The TKA is considered as the gold standard compared to other surgical procedures such as partial knee replacement (126). Although the TKA is performed for patients with end-stage radiographic knee OA, the decision to operate is also guided by the patients' symptoms (126). However, there is no consensus regarding the degree of severity of symptoms to indicate need for the surgery (127). Therefore, preoperative decision-making could be a complex process for both clinicians and patients (126). However, other factors such as age and BMI are worth considering (126). Studies have shown that TKA receipients below 55 years and/or morbidly obese have more variable outcomes compared to those over 55 years and/or have a lower BMI **(128–131)**.

The need for TKA and its prevalence is increasing due to increasing age and obesity (25,132,133) with concomitant increase in prevalence of knee OA (which accounts for 94-97% of all TKAs (31)). Studies show that there is increased prevalence of TKA in knee OA patients younger than 65 years of age (134–136). In terms of gender, more women undergo TKA than men with the ratio of 1.4:1 (137). It has been reported that the number of TKAs is increasing yearly in developed countries (126). Similarly, the South African National Joint Registry (SANJR) Annual Report in 2016 (33) revealed that, TKA is increasing in South Africa with higher occurrence in women (61%) than men. The report also showed that TKA is predominant in adults aged 55-74 years and over 50% of the patients had BMI between 30 and 42 kg/m^2 and 94.5% of the TKAs were due to knee OA (33).

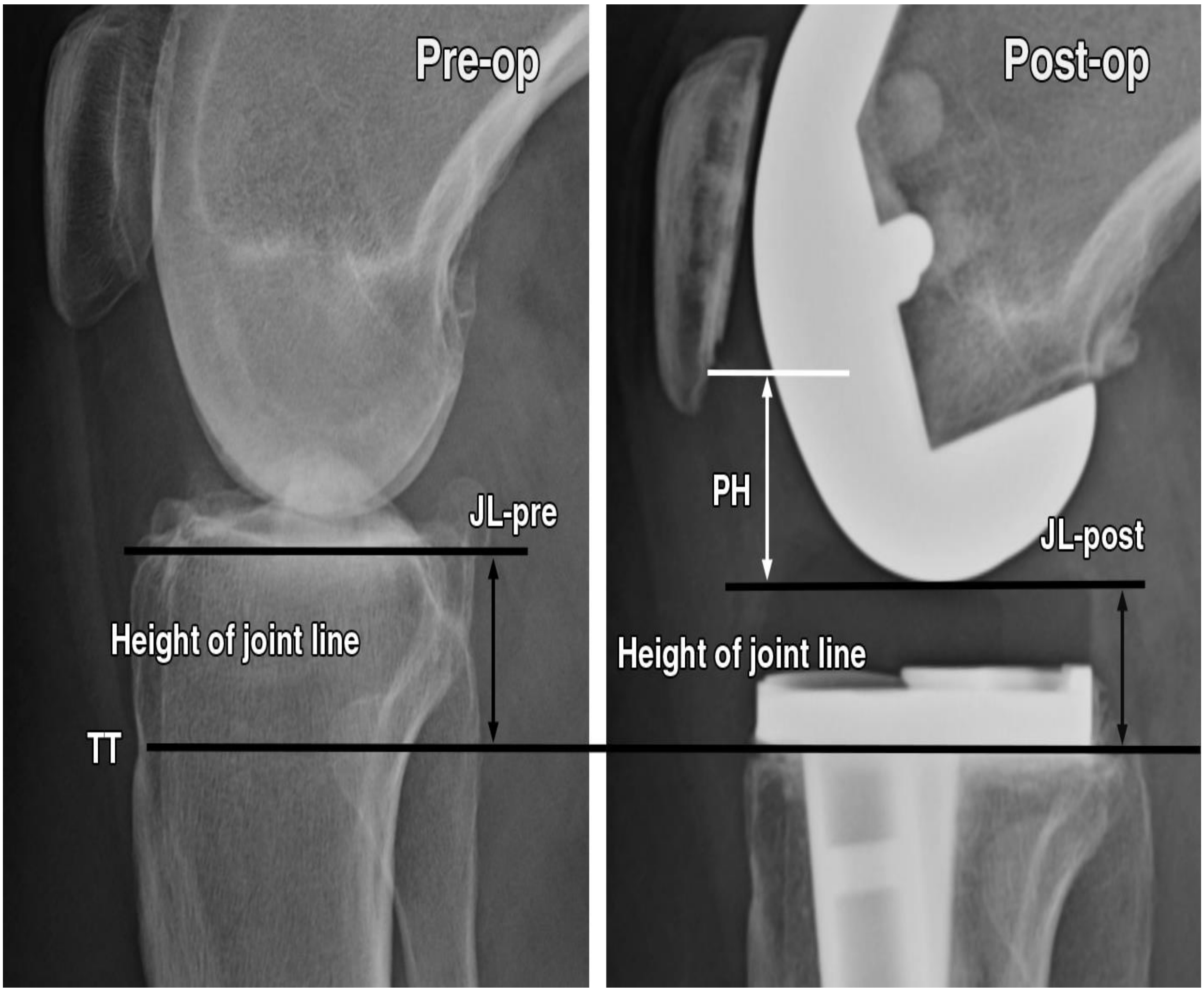

Figure 1. 3 Radiographs showing knees before TKA (left) and after TKA (right).

TT- tibial tubercle; PH- Patella height; JL- joint line (138).

1.8 Health outcomes before and after TKA

Majority of patients with OA have movement disabilities with 25% unable to perform major ADLs where 11% of knee OA adults require assistance with self-care and 14% needing help with routine daily activities (16). The knee OA-associated pain results in the limitations in performance of ADLs and poor QoL (16). Total knee arthroplasty results in substantial improvements in health outcomes measured subjectively using PROMs including those for pain, physical functional performance and QoL as well as PA rating (29,41,53,57,58,139,140).

The PROMs subjectively measure health outcomes before and after TKA (29). As improvements in QoL and FC are the most essential outcomes following TKA, the perception of patients regarding these outcomes are important (141). However, the PROMs differ in the number of domains they assess (142). The WOMAC and SF-36 assess pain, stiffness, and physical function in patients with hip and knee OA and have been used in some longitudinal studies on patients undergoing TKA (29,143). The KOOS has been used to assess pain, ADLs, sport and recreational function and knee-related QoL (144,145). The OKS has been used to assess pain, physical functioning, disability and QoL in knee OA patients following TKA (40,146,147).

Although PROMs are easy to administer, inexpensive, save time, do not need special training and may reduce drop out of participants to follow up in studies (139), they are subjective or lack objectivity, unreliable, biased regarding recall and have a ceiling effect (49,148). Another problem with using PROMs is that patients may exaggerate their health outcomes and that self-reported improvements do not correlate with objective measures such as performance-based measures (for example, timed-up-and go, chair-rise and six-minute walk tests) (145). Thus, PROMs may not capture the actual change in physical functional performance following TKA (149,150). Furthermore, PROMs show considerable improvements following TKA but very little or no improvements in objectively measured PA have been reported (54,55). However, the discordance between objectively measured PA and PROMs following TKA has not been well studied. In addition, more objective, reliable and quantified data are needed to demonstrate the effects of TKA on overall physical functioning. Objectively assessing improvements in functional ability following TKA would enhance the assessment of success as well as cost-effectiveness of the surgery as the need for TKA is increasing.

1.9 Activity behaviours and health in knee OA patients

1.9.1 Brief introduction to physical activity and sedentary behaviour

The day (24-hour period) is made up of periods of sleep, SB and PA of all intensities including light physical activity (LPA), moderate and vigorous physical activity (MVPA) (52,69,151). Typically, adults spend 31% (7.5 hours) of the day sleeping, 39% (9.4 hours) in SB, 27% (6.5 hours) in LPA and 3% (43 mins) in MVPA (moderate 2.5% and vigorous PA 0.5%) (70). These activity behaviours interact to influence overall health (69,152).

Physical activity is any bodily movement produced by skeletal muscles that requires energy expenditure (153). Physical activity may be classified as an exercise or incidental PA (154). Therefore, exercise is a structured, planned and purposeful PA performed to promote health and physical fitness (153). However, incidental PA is not planned but occurs spontaneously in activities of daily routines at home, work and during transport (154). Physical activity increases energy expenditure above resting levels and the rate of energy expenditure is directly related to the intensity of the PA (154). Hence, PA is normally quantified by measuring the amount of energy expenditure in kilocalories or by metabolic equivalent (MET), where one MET is the resting energy expenditure at rest and is equivalent to 3.5 $mLO_2 \cdot kg^{-1} \cdot min^{-1}$ or ≈250 mL/min of oxygen consumed for an adult of average body weight (154). Based on intensity PA may be classified as LPA and MVPA if energy expenditure is equivalent to 1.6-2.9 METs and MVPA ≥3 METs respectively (72,155). The current (2018) American PA guidelines for adults including those with knee OA, recommend participation in 150 to 300 mins of MVPA per week (156). Achieving the PA guidelines has several health benefits including improvements in physical fitness, prevention of chronic diseases and decreased risks of mortality (67,157). The current PA guideline was developed after a thorough review of scientific evidence since the 2008 PA guideline (158). Although, the 2008 PA guideline was excellent (158), the current PA guideline builds on it and has expanded the knowledge about the relationship between PA and health over the past decade (156). This current PA guideline (156) provides scientific evidence of even more health benefits and demonstrates greater flexibility regarding meeting the PA guidelines and the associated health benefits than the 2008 guideline (158). For example, the current PA guideline clearly states that there is no threshold beyond which health benefits occur and that any amount of MVPA counts towards meeting PA guidelines (156) (as opposed to the bout length of at least 10 mins of MVPA in the 2008 PA guidelines (158)). Nonetheless, inactive individuals can achieve greater health benefits by reducing SB or increasing MVPA or both (156).

Sedentary behaviour is defined as any waking behaviour characterised by an energy expenditure of 1.0 to 1.5 metabolic equivalents (MET) while in a sitting or reclined posture (159–162). Sedentary behaviour is a different activity behaviour construct from physical inactivity, which is defined as not meeting the PA guidelines) (162–164). Studies have shown that individuals who accumulate large amounts of SB have high risk of health consequences (such as morbidity and mortality) regardless of their MVPA levels (159,165–168). Thus, an individual can accumulate high levels of both SB and MVPA over the 24-hour period (166,169–172). Examples of SB include time spent sitting, reclining or lying while using electronic devices (such as television, computer, tablet, phone), reading, writing or talking, or sitting in a bus, car or train (164). Sitting is the most common SB of adults and individuals can sit for prolonged hours at a time in a day (173). Matthews et al (174) observed in the 2003–2004 National Health and Nutrition Examination Survey (NHANES) that their participants (healthy adults) spent 55% of the waking time sedentary.

Studies have shown that SB is associated with increased waist circumference, systolic blood pressure, fasting blood glucose, triglycerides, impaired glucose metabolism, (169,175) and type 2 diabetes as well as increased premature, all-cause and cardiovascular disease mortality rates in adults (176–179). People with knee OA are at a higher risk of experiencing these co-morbidities due to the functional limitations that they experience.

1.9.2 Measurements of physical activity and sedentary behaviour

1.9.2.1 Physical activity questionnaires

Physical activity is a complex activity and health behaviour comprising multiple dimensions (i.e., frequency, intensity, duration and type) and domains (including domestic/household, occupational, transportation and leisure time), therefore, good PA measurement should provide a valid and reliable estimate of the dimensions and domains (61). Physical activity is measured both subjectively and objectively (180–184). The subjective measures used to assess PA include self-report questionnaires,

diaries, logs and recalls (180–184). Although a plethora of questionnaires for measuring PA are available, most of these PA questionnaires were primarily developed and have been validated for assessing PA of the general population rather than in clinical populations (35).
The PA questionnaires commonly used for measuring PA of patients with knee OA are the International Physical Activity Questionnaire (IPAQ), Short Questionnaire to Assess Health-Enhancing Physical Activity (SQUASH), Baecke Physical Activity Questionnaire (BPAQ), Lower-Extremity Activity Scale (LEAS), Visual Analog Scale (VAS) for patients and physicians, Tegner Score, Physical Activity Survey for the Elderly (PASE) and the University of California Los Angeles (UCLA) Activity Index (35,45,47,67,140,185,186).

The UCLA activity index is a common activity questionnaire for assessing patients undergoing total joint arthroplasty (35,185,186) and hence, may enable comparison between studies (35). The UCLA has 10 items describing the activity levels of patients from one (1) to 10, where 1 denotes "wholly inactive, dependent on others and cannot leave residence" and 10 means "regularly participates in impact sports". However, in one study, the UCLA activity index was sub-classified into sedentary (1-2), mildly active (3-4), moderately active (5-7) and highly active (8-10) (44). Naal et al (186) showed that the UCLA activity index differentiated between insufficiently and sufficiently active patients with hip or knee OA scheduled for total joint arthroplasty.

Generally, PA questionnaires (including UCLA) are cheap, readily available, easy to administer, desirable for large-scale epidemiological studies over a short period of time at a low cost and applicable across the age group (182–184,187). However, similar to the PROMs, PA questionnaires also have several limitations including poor validity and reliability, biased regarding recall and recall may be influenced by memory impairments in older adults, inability to capture all activity patterns and may underestimate or overestimate activity (181–184,187). The PA questionnaires have low reliability and validity for estimating energy expenditure (188). In addition, PA questionnaires do not have definitions for minimal important change and also do not assess different postures (35), which may be important in patients with knee OA and/or undergoing TKA who make smaller movements. Furthermore, there appears to be a poor association between objectively measured PA and self-reported PA (39,40,185).

1.9.2.2 Sedentary behaviour questionnaires

Similar to PA, self-report questionnaires are the most common measures used for assessing SB compared to face-to-face and telephone methods (189,190). The questionnaires are important for assessing the context of sedentary time and identifying specific types of SB (such as TV viewing, reading, computer use and driving) (191). Television (TV) viewing time is the commonly used SB measure as a surrogate or proxy marker of overall SB (48,189,190). However, TV-viewing time may not capture total SB and is underreported when compared with objective measures (189,190). Some questionnaires globally assess SB using the daily total time spent sitting (48). For example, the IPAQ has one item assessing the time spent sitting, however, a single-item question may underestimate or overestimate time spent sitting (192).

While there may not be questionnaires specifically developed to measure SB in patients with knee OA and/or undergoing TKA, one study used a previously validated questionnaire, the Longitudinal Ageing Study Amsterdam (LASA) Sedentary Behaviour Questionnaire (193) and the seven-day Sedentary and Light Intensity Physical Activity Log (SLIPA) to measure sedentary time in addition to accelerometry measurements in pre-TKA and post-TKA patients (59). The findings showed there was no correlation between both the objectively measured sedentary time and sedentary time measured subjectively. However, the responses on the LASA and SLIPA were associated with each other but tended to underestimate low amounts of sedentary time and overestimate high amounts of sedentary time compared with objective measures (59). Objective measures (such as accelerometers) provide a valid, reliable and detailed assessment of SB however studies that specifically identify SB in patients with knee OA and/or undergoing TKA are lacking. Objectively assessing changes in SB following TKA would more accurately increase our understanding about the patterns of SB and their impact on patients following surgery as well as the understanding of how to develop targeted interventions for improving SB of patients after the surgery.

1.93 Objective measurements of physical activity and sedentary behaviour

1.9.3.1 Accelerometers

There are several methods for measuring PA including wearable activity monitors (such as accelerometers and pedometers, heart rate monitors and combined sensing or multi-unit monitors), calorimetry, direct observation and doubly labelled water (180–184). However, for the purposes of this thesis the focus will be on accelerometers. This is because accelerometers can reliably measure detailed patterns of PA and SB as these activity monitors capture the frequency, intensity and duration of movement in a time-stamped manner (154,194).

In recent times, accelerometers have become the most commonly used devices for measuring PA and SB in free-living populations (195). Accelerometers are small light-weight devices and are worn either at the hip, back, thigh, ankle or wrist (48,154,196). Accelerometers measure accelerations of body movements and also capture the frequency, intensity and duration of movement in a time-stamped manner (154). The accelerations may be measured in one to three orthogonal planes: either on one plane (usually in a vertical), two planes (vertical and mediolateral or vertical and anterior-posterior) or three planes (vertical, mediolateral, and anterior-posterior) (195,197). The majority of accelerometers have piezoelectric sensors (182). When the sensor detects or undergoes acceleration, the seismic mass causes the piezoelectric element to experience mechanical deformation by bending or undergoing compression (197). The conformational changes cause the displaced charges to build up on one side of the sensor, generating a variable output voltage signal whose amplitude is proportional to the applied or detected acceleration (195,197).

Accelerometers generate a measure of activity intensity known as '*counts*' (raw movement signal or output) (195,197). The counts can be used to determine energy expenditure and classify activities into different levels (183). The accelerometers also directly measure the number of steps per day (196,198). Very importantly, accelerometers are useful in describing activity patterns in a day or over a week (196). Accelerometers can be reliably used to estimate the proportion of people meeting the PA guidelines (199–201), the length and number of activity bouts

(199,201), breaks or interruptions in sedentary time (202), or transitions between sitting and standing (203).

Methodological considerations

There are several methodological considerations in using accelerometers in terms of choice, placement, number of days of accelerometer wear and data processing. The choice of accelerometer for studies may depend on the primary outcome of interest, reduction of participants' burden (in terms of number of monitors to be used, placement, and length of wear time), memory capacity of the monitor, supply costs and technical support available for data processing (182). Accelerometry output depends on placement of monitor, its orientation, posture and activity being performed (204). For measuring PA, accelerometers are best placed on the hip or lower back as close to the body's centre of mass as possible (61). However, placing the accelerometer on the thigh is preferable for generating accurate estimates of SB and patterns of sedentary time accumulation since the thigh changes position during transitions from sitting/lying to standing (205). It has been recommended that three to seven days of accelerometer wear times are needed to generate activity data likely to be representative or typical of individuals or the population being studied (61). For a day to be counted valid for accelerometer wear, there should be ≥10 hours per day (600 mins/day) of waking wear time (206). It is important that both week and weekend days are included as studies have shown differences in patterns of activity between these two types of days (207). It is recommended that at least three weekdays and one weekend day should be included (206). In most accelerometers, it is important to classify or define both wear and non-wear time intervals (208). The non-wear times are periods during which participants are asked not to wear their accelerometers including showering, sleeping and swimming and periods when participants forget to wear monitors after removal (208).

One important issue for consideration in using accelerometers is the *epoch length* for measuring activity. The epoch length is the filtered digitized acceleration signal over a user-specific time interval (61). The epoch length is essential in determining the amount of time spent in different activity intensities and therefore should be specified a priori to activity data collection (61). A one-minute (60-second) epoch length has been used in studies measuring activity or energy expenditure in adults (61). This is because accelerometers previously had low data storage capacity and were able to store data collected with epoch length of <60s for limited number of days (61), however, a one-minute epoch length may be inappropriate for measuring PA of children whose activities occur in short bouts (157,209). When data are collected with motion-based accelerometers (such as an ActiGraph) cut-points are used to classify epoch as SB or PA (LPA and MVPA) but not when a posture-based monitor (such as an ActivPAL) is used (205). The most commonly used cut-points include those where activity is classified sedentary if less than 100 counts per minute (cpm) (174), light intensity activity if between 100 and 1951 cpm, moderate-vigorous intensity activity if between 1952 and 5724 cpm and vigorous if greater than 5724 cpm (210). Currently, assumptions for the choice of cut-points and data analysis are not standardized across studies or populations (211).

Advantages and Limitations

The objective measures are designed to overcome limitations of the PA and SB questionnaires (182). Unlike subjective measures, accelerometers offer a more accurate, reliable and valid estimate of activity behaviours in a free-living environment since they do not depend on information from participants and are not subject to recall bias and ceiling effects (195). Some accelerometers accurately measure and distinguish body postures (212) and also measure low intensity activities incidental in ADLs (195), which may not be measured with PA questionnaires (213). Accelerometers provide comprehensive information on activity in terms of intensity, frequency and duration (214) and may be better used to assess participants' compliance to PA guidelines than using PA questionnaires. Therefore, accelerometers can increase our understanding and knowledge base of PA in older adults beyond time spent in MVPA (213). Another limitation of accelerometers is that, the monitors cannot measure or distinguish between the domains or contexts of the activity, that is, household, leisure time and walking for transportation (154,195).

Objectively measuring PA with accelerometers may provide an alternative means of assessing improvements in functional ability in knee OA patients following TKA (215). Accelerometers may provide a more quantitative and accurate estimate of the effects of TKA on PA and functional ability in patients with knee OA than the PA, SB and knee-specific mobility questionnaires. Functional ability may have improved where a change in ADLs (assessed using objectively measured SB and LPA) occurs without a change in MVPA (215). Using both motion-based and posture-based accelerometers may provide detailed information on activity behaviour patterns of patients with knee OA that would better allow for studying impact of PA and SB on health.

Unlike PA and knee-specific mobility questionnaires, accelerometers are expensive, need special training for collecting and analysing data (194). The absence of standardised methods for data reduction limits comparisons of findings across studies (61). Finally, achieving data completeness becomes problematic especially when waist-worn accelerometers are removed before showering or bathing and swimming (61) or when participants forget to wear accelerometers after removal (208). These may result in insufficient data for describing activity behaviours. Table 1.1 summarises some of the commonly used accelerometers and their methodology in public health and clinical studies. However, for the purpose of this thesis, two of the accelerometers are highlighted in the next section.

1.9.3.1.1 ActiGraph Accelerometer (ActiGraph GT3X+)

ActiGraph accelerometers are the most widely used motion-based wearable monitors for measuring PA (206). The earlier models of ActiGraph monitors (ActiGraph, Pensacola, FL, USA) were formerly known as Computer Science and Application (CSA) and Manufacture Technology Incorporated (MTI) (216). However, these early models of ActiGraph were uniaxial accelerometers and hence, could only detect accelerations on the vertical axis (217).

In 2009, ActiGraph released the new generation of ActiGraph called ActiGraph GT3X+ accelerometer (217). The GT3X+ provides activity counts as a composite vector magnitude (VM) from the three axes (218). The ActiGraph GT3X+ accelerometers allow for a more accurate measurements of PA, particularly MVPA (219) and provide a more comprehensive measurement of PA than their earlier models (197,220). Specifically, ActiGraph GT3X+ provides data on PA including activity counts, energy expenditure, activity intensities- METs (SB, LPA and MVPA) and step counts (220) (Table 1.1). A unique feature of ActiGraph GT3X+ is its inclinometer function to detect postures or body position (such as sitting, lying and standing) and to identify periods of non-wear (220). The incorporation of an inclinometer makes ActiGraph GT3X+ also useful for measuring SB patterns.

The ActiGraph GT3X+ has been used to measure PA and SB of older adults (221–223). The activity monitor has been validated for measuring energy expenditure (220), SB and LPA (224), postural allocations (such as sitting, lying and standing) in older adults (73). However, compared to the ActivPAL, ActiGraph GT3X+ was less sensitive to reductions in sitting time and changes in absolute number of breaks in sedentary time and break rate (51,225). ActiGraph GT3X+ is a hip-worn accelerometer and therefore, has a difficulty of discriminating sedentary activities based on posture (226). For instance, ActiGraph GT3X+ is unable to accurately differentiate between sitting and standing (205,226). This methodological challenge stems from the fact that the ActiGraph, quantifies time spent in different intensities of PA by summing time above and below specified count thresholds. Therefore, the ActiGraph accurately measures MVPA, but it less accurately distinguishes between sedentary activity (sitting) and LPA (standing) (227).

1.9.3.1.2 The ActivPAL (Inclinometer)

Another commercially available wearable activity monitor that is increasingly being used in activity behaviour studies is the ActivPAL accelerometer (PAL Technologies Ltd) (Table 1.1). The ActivPAL is a small light-weight uniaxial inclinometer that detects and measures postures (48). The ActivPAL is worn on the midline of the anterior thigh that uses information from static and dynamic accelerations to distinguish body posture as sitting/lying (sedentary behaviour), standing and stepping/walking (228) as well as estimate energy expenditure (EE) (expressed as METs) (229). The ActivPAL uses inclination of the thigh to determine the start and end of each period spent sitting/lying, standing and stepping, as well as average daily cadence, step counts and postural transitions in free-living activities or behaviours (219,229,230). Thus, the inclinometer is not typically used to determine SB as measured with the ActiGraph GT3X+ (which is based on counts, usually <100 cpm), but it measures SB by posture with inclinometer value. Unlike ActiGraph GT3X+, the ActivPAL accurately distinguishes standing still from sitting time (205,230) and it is sensitive to a reduction in time spent sitting or sedentary in active healthy adults (51,231). Therefore, a unique functional distinguishing feature of the ActivPAL is its ability to measure low intensity activities (sitting or sedentary time, standing and walking).

The ability of the ActivPAL to accurately measure low intensity activities is essential in patients with musculoskeletal deficits, since these activities can be sustained for much longer periods of time than higher intensities (72). Moreover, patients with knee OA are more likely to be less moderate-vigorously active but highly sedentary as a result of the disease-associated symptoms and disabilities (74). The ActivPAL was demonstrated as a reliable and valid device for measuring step counts and cadence in older adults (232) with slow average daily cadence (233). The device was validated for use in measuring energy expenditure, walking time and total activity in healthy and in-patient older adults (234). The ActivPAL was found to be feasible in measuring activity patterns (sitting/lying, standing and stepping) in older adults in residential care homes (235). However, the ActivPAL does not distinguish between sitting and lying (236). Moreover, a review concluded that more detailed guidelines are needed for consistently reporting ActivPAL activity data across studies involving older adults (237).

Using both ActivPAL and ActiGraph GT3X+ for measuring different aspects of activity behaviours would allow for a richer and more detailed analysis of PA and SB in patients with knee OA and/or undergoing TKA. Such data would generate better evidence of improvements in daily activity (and therefore a surrogate measure of daily functional ability) of patients following TKA compared to the functional questionnaires. These data would enhance effective treatment of patients with knee OA undergoing TKA as the data could inform targeted interventions for improving PA and decreasing SB both at pre- and postoperatively (238).

Table 1.1 Summary of the most commonly used accelerometers for objective measurements of physical activity and sedentary behaviour

Name	**Manufacturing Company**	**Type of technology**	**Size/weight**	**Epoch length**	**Data recording capacity**	**Placement/ wear site**	**Activity outcome measures**
ActiGraph wGT3X+-BW	ActiGraph LLC Pensacola, FL	Triaxial	4.6x3.3x1.5 cm/ 19 g	1 sec. – 1 min	19 days	Hip, ankle, wrist	Activity counts, PA intensity (LPA, MVPA), SB, energy expenditure, step counts.
ActivPAL	PAL Technologies Ltd., Glasgow, UK	Triaxial inclinometer	5.1x3.6x0.8 cm/ 20.1 g	1 sec. – 1 min	10 days	Midline of anterior thigh	Sitting, standing, stepping, step counts, step rate, energy expenditure.
AMP-333	Activity Monitor Pod, Dynastream Innovations Inc., Cochrane, AB, Canada	Biaxial	7.1x2.4x3.8 cm/ 50 g	1 min	1-4 days	Ankle	Steps, cadence, walking speed, stride length, distance, energy expenditure
ActiGraph Model 7164 (formerly CSA, MTI)	ActiGraph LLC Pensacola, FL	Uniaxial	5.1x4.1x1.5 cm/ 45.5 g	5 sec. – 1 min	22 days	Hip, ankle, wrist	Activity counts, PA intensity energy expenditure
ActiGraph Model GT1M	ActiGraph LLC Pensacola, FL	Uniaxial	3.8x3.7x1.8 cm/ 27 g	5 sec. – 1 min	22 days	Hip, ankle, wrist	Activity counts, steps
Actical	Mini-MitterSunriver, OR	Uniaxial, Omni-directional	2.8x2.7x1.0 cm/ 17.5 g	5 sec. – 1 min	45 days	Wrist, hip, ankle	Activity counts, step counts, energy expenditure
Actiheart	Cam *n*tech	Uniaxial	3.2 x 0.6 cm/ 10 g	15 sec. – 1 min	21 days	Anterolateral chest	MVPA time, physical activity energy expenditure (PAEE)

Actiwatch	Mini-MitterSunriver, OR	Uniaxial, Omni-directional	2.8x2.7x1.0 cm/ 16 g	15 sec. – 15 min	11 – 45 days	Hip, wrist	Activity counts, sleep quality
Biotrainer Pro	IM Systems, Baltimore, MD, USA	Biaxial	7.6x5.0x2.2 cm/ 51.1 g	15 sec. – 5 min	22 days	Hip	Activity counts, steps, PA intensity, energy expenditure
Dynaport Activity Monitor	McRoberts BV, The Hague, The Netherlands	Triaxial	8.5x5.8x11.5cm/ 55	1 sec. – 1 min	7 days	Middle lower back + one leg sensor (thigh)	Step counts, energy expenditure, PA intensity, lying, sitting, standing, walking
GENEActiv	Unilever Discovery, Sharnbrook Bedfordshire, UK	Triaxial	3.6x3.0x1.2 cm/ 16 g	-	8 days	Wrist, waist, ankle, hip, thigh	Physical activity, posture, vector magnitude unit, energy expenditure
IDEEA (Intelligent Device for Energy Expenditure and Activity)	MiniSun, LLC, Fresno, CA, USA	Biaxial	7x5.4x1.7 cm/ 59g (recorder) + 1.8x1.5x0.3 cm/ 2 g (sensors)	1 sec. – 1 min	7 days	Waist (processing unit) + both feet, both thighs and chest (sensor)	Energy expenditure, activity type, speed, distance, power output

PA: physical activity; MVPA: moderate-vigorous physical activity; PAEE: physical activity energy expenditure; SB: sedentary behaviour; LPA: light physical activity; g: acceleration due to gravity; CM: centimetre; CSA: Computer Science and Application; MTI: Manufacture Technology Incorporated; IDEEA: Intelligent Device for Energy Expenditure and Activity. Adapted from previous studies (154,182,219,238,239).

1.10 Physical activity and health in knee OA

Sufficient PA is important for people with knee OA as the risk of co-morbidities is already increased in this population with walking disability (240). In knee OA patients, regular PA leads to improvements in functional independence and QoL, increased muscular strength, balance, gait patterns and coordination with reduced fall risks (96,241) as well as the promotion of weight loss (242). Studies have shown that patients with knee OA participating in activities such as walking and aquatic-based programmes experience increases in aerobic capacity, functional mobility and improved pain and depression (243,244). Maintaining an active lifestyle can also improve joint health (such as increasing cartilage volume and decreasing its defects) and delay the progression of OA and the disease-associated disabilities (245,246). Dunlop et al (23) reported in their study involving 2,589 knee OA patients aged 63 years recruited from the Osteoarthritis Initiative (OAI) that, there is a relationship between self-reported PA level and better functional performance in adults with knee OA.

Despite the health benefits of adequate PA, patients with knee OA accumulate very low amounts of PA (247). In a survey of 1,713 patients with knee OA, it was reported that less than 50% of the participants walked an hour or more per week for exercise (248). Studies have shown that PA levels of patients with end-stage knee OA are lower than the recommended PA guidelines (17,67,249) with increased SB (18), when measured either subjectively or objectively. Hootman (250) found that, using self-reported PA 24.3% and 27.4% of adults with arthritis and without arthritis in the US respectively met the PA guidelines. In their study using self-reported PA, Kersten et al (67) reported that close to 50% of patients with knee OA scheduled for knee arthroplasty did not meet the PA guidelines but 64% of the control counterparts complied with the PA guidelines. Dunlop et al (249) in their study, involving 1,111 knee OA patients aged 49-84 years recruited from the Osteoarthritis Initiative (OAI) reported that objectively measured PA showed that 41.1% of males and 56.5% of females with knee OA were inactive. Similarly, using accelerometers, Lee et al (251) found that only 10.2% of their patients (out of a total of 1,089 aged 49-84 years recruited from the OAI) met the PA guidelines and 48.9% of patients with radiographic knee OA were physically inactive. Furthermore, in one study (involving 51 participants aged 68 years with BMI of 28.4 kg/m^2) objectively measuring PA with accelerometers, it was reported that only 30% of patients with early-stage knee OA met the PA guidelines (243). Additionally, when using the number of steps recommendation, 19%-48% of the participants with knee OA met the ≥7000 and/ ≥10000 steps per day recommendation (17). In a systematic review of objectively measured PA with activity monitors, Wallis et al (17) reported that between 13%-41% of participants with knee OA met the PA guidelines.

Not only do the vast majority of knee OA patients not meet the recommended guidelines for PA but they also have lower levels of PA compared to their counterparts without the disease (74,252). Herbolsheimer et al (74) observed that whereas patients with knee OA accumulated on average 62.9 mins of MVPA per day, the non-knee OA participants accumulated 81.5 mins of MVPA per day. In another study, while 31% of adults with arthritis were physically inactive, 26% of their counterparts without arthritis were inactive (250). Furthermore, between 2008 and 2015, the percentage increase of participants with arthritis being active (3%) was lower than those without arthritis (7%) (253).

The decreased PA levels in patients with knee OA may be attributed to pain (254–256), obesity (73,251,257), ageing (258,259) and joint injury (101,260). Lee et al (251) observed that overweight, obesity, inadequate dietary fibre intake, severe knee dysfunction and severe knee pain were significantly associated with physical inactivity. With increasing age, PA decreases significantly and individuals may become more sedentary (261). Furthermore, despite all that limits PA in knee OA patients, weight loss is feasible at all stages of the disease (262). Aside from the patient-specific factors mitigating PA levels in patients with knee OA, social, environmental, and other factors may impair PA levels in patients with knee OA (74). However, with supportive infrastructure or culture, low intensity activity (such as walking) can accrue high levels of PA with lesser contribution from vigorous activity (263). Furthermore, the 2018 PA guidelines recommend that substituting SB with LPA in people not meeting the PA guidelines reduces risks of chronic diseases and all-cause mortality (264). Since knee OA is prevalent among the ageing population coupled with the disease-associated disabilities, knee OA patients are at risk of much lower PA level and increased SB compared to adults without OA. Therefore, interventional strategies (both clinical and psychosocial) that would improve PA levels of patients with knee OA are needed.

1.11 Sedentary behaviour and health in knee OA

An increased time spent sedentary can result in increased risk of sarcopenia (loss of skeletal muscle mass and strength) in healthy older individuals (265) whereas frequent breaks in sedentary time can lead to a better skeletal muscle quality in older men (266). In patients with knee OA, high levels of SB were associated with elevated blood pressure (22), severe loss of physical function (18) and weight gain (20). A study reported that 1,168 older adults with knee OA aged 66 years spent two-thirds (67%, 9.8 hours/day) of their waking time sedentary (18), which is similar to the levels reported for older adults without knee OA (65-80% of waking day, 9.4 hours/day) (267). Other studies have also reported that adult knee OA patients spend 50% of the waking day watching TV or in other sedentary activities (173,200). Large amounts of time spent in SB have been found to be an independent risk factor for not only cardiometabolic diseases but also musculoskeletal health problems and all-cause mortality (167,178,179,268). Lee et al (18) demonstrated that being less sedentary was associated with better physical function in adults with knee OA independent of MVPA time. In another study, a strong association was demonstrated between SB and increased systolic and elevated blood pressures, independent of time spent in MVPA (22). On the other hand, a small increase in MVPA and decrease in sedentary time over two years were associated with weight loss among adults with obesity and with or at increased risk for knee OA (20). Chastin et al (269) demonstrated that breaks from sedentary time were associated with improved muscle quality in older men and that those who were more sedentary experienced greater functional capacity loss compared to adults who were less sedentary independent of MVPA (18,21,270). The implication of the aforementioned findings support guidelines to encourage adults with knee OA to decrease time spent in SB in order to improve physical function (18) and overall health.

Studies specifically focusing on SB in knee OA patients are lacking and very few studies have reported some aspects of SB in patients with knee OA undergoing TKA (56). The fact that SB is an independent health risk and since large volumes of SB predispose to musculoskeletal and cardiometabolic health problems and mortality, independent of MVPA (167,178,179,268), more SB studies in patients with knee OA are required. This would enable better studies of the health effects of SB in patients with knee OA.

1.12 Activity behaviour in knee OA patients before and after TKA

Older adults with knee OA have a decline in physical function and prolonged periods of muscular unloading accelerate losses in muscle and bone mass (191). These increase the risk of falls, frailty and dependence in older adults (191). Older adults engage more in low intensity activities (SB and LPA) throughout the day with very few of them performing high intensity activities (184). Thus, SB and LPA are common among older adults at home, work and during leisure (271,272). Studies showed that on average older adults spend approximately 60–70% of their waking day in SB (227,273). A review of studies across 10 countries demonstrated that older adults spent over 10 hours of the day sedentary (267) compared to the younger age groups (174,274).

Offsetting SB by promoting an increase in LPA may be a feasible approach to ameliorating the deleterious health consequences of low activity due to knee OA (173). Decreasing sedentary activities must involve an increase in activities that are less intensive than MVPA as many people with knee OA are unable to engage in enough MVPA (275). Furthermore, LPA is more consistent with purposeful movements accumulated during performances of ADLs (151,69). Postural changes or transfers from sitting to standing and/or walking have also been found to significantly increase energy expenditure (276). Buaman et al (263) reported that objectively measured LPA was significantly associated with better health outcomes in older adults over 65 years. Other studies have shown that decreasing time spent sedentary and increasing LPA may be important for improving cardiometabolic health in adults independent of MVPA [63,64]. Therefore, LPA (such as walking) can provide important health benefits (69) before and after TKA; however, this has received little attention in studies compared to MVPA (which does not change following the surgery).

Low intensity exercises have been recommended to be beneficial for knee OA patients (279), as they are at the lower end of the activity continuum (161). Lifestyle strategies that target at displacing sedentary time (sitting) with LPA or incidental PA such as standing or walking may be of great benefits (227). A shift from SB to LPA may have public health benefits since a greater percentage of the population do not even meet the PA guidelines (227). Furthermore, increased daily walking is associated with less risk of functional limitation over two years and is more likely to protect against development of functional limitations in patients with TKA (246) justifying the importance of increasing activity, even if it is of a lower intensity, after TKA.

Table 1.2 summarises studies that used accelerometers to describe and quantify activity behaviours before and after TKA. The first study that objectively measured PA with an accelerometer (Numact Activity Monitor) in patients with knee OA undergoing TKA was published in 2002 (62). This seminal work has revolutionised activity behaviour assessments in patients with knee OA undergoing TKA. Nonetheless, few studies have used accelerometers to measure PA of patients with knee OA before and after TKA.

Studies assessing PA of patients undergoing TKA have mainly originated in high-income or socioeconomic countries including Australia (40,280), Canada (59), Germany (53,64,68), USA (57,58), UK (62) and The Netherlands (39,42,146). However, industrialisation with improved economic status can predispose people to sedentariness (281,282). Therefore, measuring PA and SB of people with musculoskeletal problems such as knee OA patients from low-middle income countries before and after TKA may increase the knowledge base on activity behaviour changes following their surgery.

The majority of the studies were longitudinal studies, however, there were cross-sectional and a case-control studies that compared PA of patients awaiting TKA and postoperative TKA patients (57–59,280). As expected, females constituted a greater proportion of the study populations compared to males. Patients ranged in age from 49 to 73 years with a BMI between 29 kg/m^2 and 35 kg/m^2.

The ActiGraph accelerometers were used in most of the studies. Whereas the uniaxial GT1M ActiGraph was used in three studies (40,57,58), the triaxial ActiGraph GT3X+ has been used in only one study to date (59). The ActivPAL has been used in two studies (64,68). Different measures of PA have been used to assess patients preoperatively and postoperatively including: activity counts, times spent in PA intensities, times spent standing, walking/stepping, step counts and energy expenditure. An important outcome commonly assessed is the proportion of patients meeting the PA guidelines. Postoperative assessment times vary across studies from six weeks to four years postoperatively.

The percentages of patients meeting the objectively assessed PA guidelines ranged between 4.8% and <30% (40,57,58,64,68). Activity counts used as a measure of overall PA did not increase significantly at six months postoperatively (283). However, the average number of step counts per day increased postoperatively in five studies (53,59,62,68,140) with two studies reporting improvements in MVPA steps (ie., >100 steps per minute) one year post-operatively (64,68). The objectively measured time spent walking improved at six and 12 months postoperatively in some studies (53,64,68). Furthermore, ambulatory energy expenditure also improved six months after TKA (62). In two of the studies, objectively measured time spent standing also improved at six and 12 months postoperatively (53,62). Studies objectively measuring PA of different patient groups reported on the times spent in LPA and MVPA, however, there were no difference in activity times at these intensities between pre-TKA and post-TKA patients (57–59). However, longitudinal studies categorising PA into the different intensities are lacking thereby limiting our understanding of how the patterns of PA change following TKA. Hence, studies detailing the patterns of PA in knee OA patients before and after TKA are needed.

Overall, there are conflicting and inconsistent findings on changes in PA following TKA at different postoperative follow-ups. Most of the studies measuring PA at six months after TKA showed no improvements in PA (39,40,42,280) while others reported improvements in PA (53,62). Similarly, studies assessing PA at 12 months postoperatively have also yielded mixed findings with some showing improvements in PA (53,64,68) and others no improvements in PA (59,280). However, two systematic reviews with and/or without meta-analysis on objectively measured PA in patients undergoing TKA concluded that there is no change in overall PA at six months, but a marginal improvement in PA occurs at 12 months after TKA (54,55). Furthermore, using a threshold value of MVPA as the benchmark, may be an unrealistic expectation in these patients and therefore an alternative option needs to be considered. What is missing in the literature are investigations that include SB as an outcome measure following TKA. Studies appear to have recorded SB as an aside issue and have not really regarded it as an activity that is closely related to amounts of the other behaviours on the movement continuum. In this regard a thorough review of the literature is needed to determine which studies have measured SB and whether SB changes in patients following TKA.

Although studies have reported conflicting changes in objectively measured PA following TKA, health outcomes as measured by the PROMs (for pain, physical functional ability and quality of life) usually improved significantly (39,40,42,54,55). The discordance between both objectively measured PA and PROMs may suggest that there is no association between the two constructs and this implies that the drivers of PA change are not dependent on what is clinically considered as surgical success i.e. a reduction in pain. However, the association between PA, particularly low intensity activities (which have the ability to change after surgery), and the PROMs has not been well examined. Understanding the association between low intensity PA and PROMs may clinically enhance predictions of functional outcomes postoperatively and allow clinicians to identify patients who may benefit from surgery. Therefore, there is a need to explore the association between objectively measured PA and PROMs in patients with knee OA undergoing TKA.

Table 1. 2 Summary of studies objectively measuring physical activity before and after TKA

Study (Country)	Study Design	Study Participants	Activity measurements	Outcome measures	Post-operative follow up (months)	Findings
Brandes et al., 2011 (Germany)	Longitudinal	- n: 53 - Sex: (F/M)- 34/19 - Mean age (years): 65.8 (SD: 5.8) - Mean BMI (kg/m^2): 30.7 (SD: 4.1) - Side of TKA: (L/R)- NR - Co-morbidities: NR	DynaPort Activity Monitor (McRoberts) - Valid days worn: 1 day - Mean wear time: 12.3 (SD: 1.8) hrs/day	- Locomotion, % wear time Mean - Standing, % wear time - Step counts	2, 6 & 12	- Time spent walking improved significantly - Number of steps per day improved significantly
De Groot et al., 2008 (The Netherlands)	Longitudinal April 2004 – May 2006	- n: 44 - Sex: (F/M)- 24/20 - Mean age (years): 62.1 (SD: 9.7) - Mean BMI (kg/m^2): 32.1 (SD: 5.3) - Side of TKA: (L/R)- 20/24 - Co-morbidities: NR	Activity monitor (AM) - Valid days worn: 2 days - Mean wear time: 24 hours	- Movement-related activity, % 24hour - Walking, % 24hours - Upright, % 24hour	3 & 6	No change in physical activity
Harding et al., 2014 (Australia)	Longitudinal March 1 – Oct 15, 2011	- n: 25 - Sex: NR - Mean age (years): 69.0 (SD: 8.4) - Mean BMI (kg/m^2): 32.0 (SD: 5.5) - Side of TKA: (L/R)- NR - Co-morbidities: Cardiovascular, Diabetes, Respiratory, Musculoskeletal	Unixial ActiGraph GT1M (ActiGraph LLC, Fort Walton Beach, FL, USA) - Valid days worn: 7 day - Mean wear time: 14 hours	- Activity Count - Percentage meeting PA guideline	6	- No change in physical activity - 6% met the physical activity guidelines
Hayes et al., 2010	Cross-	- n: 65	Intelligent Device for	- Energy expenditure	1.5, 3, 6 & 12	- No change in

(Australia)	sectional study of different groups of patients pre- and post-operatively	- Sex (F/M): Pre-TKA: 7/6; post-TKA: 32/24 - Mean age (years): Pre-TKA- 61.1 SD: 2.2); post-TKA- 62.2 (SD: 3.4) - Mean BMI (kg/m^2): Pre-TKA- 30.3 (SD: 2.8); post-TKA- 29.6 (SD: 8.9) - Side of TKA (L/R): pre-TKA- 4/9; post-TKA- 22/31 - Co-morbidities: NR	Energy Expenditure and Activity (IDEEA) (Minisun, Fresno, USA) - Valid days worn: 1 day - Mean wear time: 24 hears	- Time spent standing and walking and transitions between movements		energy expenditure - Times spent walking and transitions between movements decreased
Kahn & Schwarzkopt, 2016 (USA)	Cross-sectional assessing Pre-TKA and Post-TKA patients	- n: 123- Pre-TKA = 63; post-TKA=60 - Sex (F/M): Pre-TKA= 32/31; Post-TKA= 30/30 - Mean age (years): Pre-TKA= 68.4 (SD: 8.2); Post-TKA= 67.3 (SD: 8.7) - Mean BMI (Kg/m^2): Pre-TKA=29.2 (SD: 4.8); Post-TKA= 31.1 (SD: 5.3)	Uniaxial ActiGraph GT1M (ActiGraph, Pensacola, Florida) - Valid days worn: 7 day - Mean wear time: 24 hours	- Activity counts, times spent in light physical activity (LPA), moderate physical activity (MVPA). - Percentage meeting physical activity guideline	20	No change in physical activity between pre-TKA and post-TKA participants. - 4.8% to 5.3% met physical activity guideline
Kahn & Schwarzkopt, 2015 (USA)	Cross assessing patients awaiting TKA post-TKA patients (March 1 – Oct 15, 2011)	- n: 123- Pre-TKA = 63; post-TKA=60 - Sex (F/M): Pre-TKA= 32/31; Post-TKA= 30/30 - Mean age (years): Pre-TKA= 68.4 (SD: 8.2); Post-TKA= 67.3 (SD: 8.7) - Mean BMI (Kg/m^2): Pre-TKA=29.2 (SD: 4.8); Post-TKA= 31.1 (SD: 5.3)	Uniaxial ActiGraph GT1M (ActiGraph, Pensacola, Florida) - Valid days worn: 7 day - Mean wear time: 24 hours	- Activity counts, times spent in light physical activity (LPA), moderate physical activity (MVPA). - Percentage meeting physical activity guideline	20	- No change in physical activity between pre-TKA and post-TKA participants. - 5% met physical activity guideline

Lützner et al., 2016 (Germany)	Longitudinal	- n: 221 - Sex: (F/M)- 126/95 - Mean age (years): 68.1 (SD: 9.5) - Mean BMI (kg/m^2): 31.3 (SD: 4.9) - Side of TKA: (L/R)- NR - Co-morbidities: ASA Grade 3 or 4 = 43.9%	ActivPAL™ Activity Monitor (PAL Technologies, Glasgow, UK) - Valid days worn: 4 days - Mean wear time: 24 hours	- Total steps and MVPA steps per day - Walking time - %Meeting PA guidelines	12	- Physical activity improved - 30% achieved active lifestyle - 22.6% met the physical activity guideline
Lützner et al., 2014 (Germany)	Longitudinal March 2009- Sept. 2011	- n: 97 - Sex: (F/M)- 45/52 - Mean age (years): 68.9 (CI: 67.2-70.6) - Mean BMI (kg/m^2): 31.3 (CI: 30.3-32.3) - Side of TKA: (L/R)- NR - Co-morbidities: ASA Grade 1 or 2 (n=50), ASA Grade 3 or 4 (n=47)	ActivPAL™ Activity Monitor (PAL Technologies, Glasgow, UK) - Valid days worn: 4 days - Mean wear time: 24 hours	- Total steps and MVPA steps per day - Walking time - %Meeting PA guidelines	12	- Physical activity improved - 16.5% met the physical activity guideline
Schotanus et al., 2016 (The Netherlands)	Longitudinal April 2014- December 2015	- n: 20 Sex: (F/M)- 7/13 - Mean age (years): 65.5 (SD: 6.1) - Mean BMI (kg/m^2): 28.5 (SD: 5.4) - Side of TKA: (L/R)- NR - Co-morbidities: ASA I/II/III ERP 2/8/0 and OS 3/7/0	Triaxial Activity Monitor (GC Dataconcepts LLC, Waveland, USA) - Valid days worn: 4 days - Mean wear time: ≥8 hours/day	- Times spent standing, walking and standing - Step counts, cadence and sit-to-stand transitions	1.5	No change in physical activity

Vissers et al., 2013 (The Netherlands)	Longitudinal	- n: 21 - Sex: NR - Mean age (years): 63.9 (SD: 9.4) - Mean BMI (kg/m^2): 29.7 (5.0) - Side of TKA: (L/R)- NR - Co-morbidities: NR	Activity Monitor (AM) (Rottterdam AM, Vitaport Technology, The Netherlands) - Valid days worn: 2 days - Mean wear time: 24 hours	-Movement-related activity -Walking time -Standing time	6 & 48	No change in physical activity
Walker et al., 2002 (UK)	Longitudinal 3 Cohorts (2 comparative groups)	- n: 19 (TKA patients), 29 (OA on NSAID) & 14 (normal control group) - Sex: F/M – 10/9 for TKA participants - Mean age, years: F= 69 (SD: 7.8); M= 69.1 (SD: 5.0) - BMI: NR	Numact Activity Monitor - Valid days worn: 1 day - Mean wear time: 24 hours - Nottingham Health Profile (NHP)	Energy expenditure, ambulatory activity, standing time, step counts	3 & 6	Increased ambulatory activity, standing time and steps per day. Self-reported mobility decreased
Webber et al., 2017 (Canada)	Cross-sectional assessing patients awaiting TKA and postoperative patients	- n: 70 – Pre-TKA=32; Post-TKA=38 - Sex (F/M): Pre-TKA: 21/11; post-TKA: 22/16 - Mean age (years): Pre-TKA- 67.9 (SD: 7.3); post-TKA- 69.9 (SD: 5.3) - Mean BMI (kg/m^2): Pre-TKA- 32.7 (SD: 6.7); post-TKA- 30.5 (SD: 6.1) - Side of TKA: NR - Co-morbidities: NR	ActiGraph GT3X+ (ActiGraph, Pensacola, FL) - Valid days worn: 7 days - Mean wear time: 13.9 (SD: 1.1) – 14.4 (SD: 1.1) hours/day	- Times spent in light and moderate to vigorous physical activity - Step counts	12	Marginal increase in physical activity in postoperative patients compared to patients awaiting TKA.

SD: Standard Deviation; IQR: Interquartile Range; F: Female; M: Male; L: left; R: right; NR: Not Reported; CPM: counts per minute; OA: Osteoarthritis; TKA: Total Knee Arthroplasty

1.14 Summary and objectives

Patients with knee OA participate in insufficient amounts of PA and spend a large amount of time in SB. Only a small proportion of knee OA patients meet PA guidelines. Following TKA, PA of patients does not appear to improve at six months but a marginal improvement occurs at one year postoperatively. Nonetheless, the literature is scant. Studies that have objectively measured PA of patients undergoing TKA have all originated in high-income or socioeconomic populations and no studies have as yet been published on patients from low to middle income countries. Therefore, there is a need for data on PA of patients undergoing TKA from low to middle income countries such as South Africa. This is important because the drivers of change in physical activity may be different in different populations. Few studies have investigated the detailed patterns by which patients with knee OA accumulate PA before and after TKA, with a specific regard to looking at all activity behaviours. This may be one of the reasons why there is inconsistency in reported changes in PA following TKA. Assessing the patterns of activity behaviours with respect to the overall volume, patterns and daily variation of activities before and after TKA would provide rich information to better study the impact and relevance of surgery on functional ability, quality of life and overall health. Moreover, the associations between objectively measured activity behaviours (including SB) and PROMs (for pain, physical function and quality of life) need to be studied in patients with knee OA undergoing TKA. This is because the PROMs are the most used measure of surgical success by clinicians in this patient population. Examining the associations between objectively measured PA, particularly low intensity activities (sitting, standing and walking/stepping) of daily life and PROMs is important since low intensity activities occur during performances of ADLs and constitute the major proportion of activities of older adults. It is important to see what the relationship is between activity behaviours and the self-report methods so that the measure of success of surgery can be supported by changes in actual relevant habitual activity behaviours in daily life following TKA.

The overarching questions that gave rise to this thesis are: (1) in other studies that have measured SB in knee OA patients, does SB change following TKA? (2) does the volume and pattern of PA and SB of patients with knee OA in South Africa undergoing TKA improve and what proportion of these patients meet PA guidelines? and (3) what are the associations between changes in objectively measured low intensity activities and changes in PROMs? The thesis is therefore centred on these questions which make up the three objectives/aims of the thesis, the rationale and aims of which are outlined below.

<u>Objective 1 – To conduct a systematic review investigating whether sedentary behaviour changes in patients with knee osteoarthritis after total knee arthroplasty:</u>

There are no published studies synthesizing findings of the available evidence that subjectively and/or objectively measured changes in SB following TKA. Therefore, the first objective of the thesis was to integrate the available evidence on changes in SB in patients with knee OA after TKA in a systematic review (56).

Objective 2 – To determine the changes in volume and pattern of objectively measured physical activity and sedentary behaviour following total knee arthroplasty:

There are no published data on objectively measured PA and SB in patients with knee OA undergoing TKA from low-middle income countries such as South Africa. The few published longitudinal studies objectively measuring PA and SB have not reported the detailed patterns by which patients with knee OA undergoing TKA accumulate PA and SB before and after a primary TKA. The majority of patients with knee OA do not meet the PA guidelines. Additionally, conflicting and inconsistent findings have been reported at different postoperative follow-ups.

Therefore, the second objective was to comprehensively describe changes in the volume and pattern of activity behaviours (PA and SB) using accelerometry in patients undergoing TKA and to assess changes in the PROMs following TKA. First, it was hypothesized that the volume and pattern of PA and SB would not change at six months after TKA. The second hypothesis was that the PROMs would improve at six months after TKA.

Objective 3 –To determine objectively measured changes in sitting, standing and walking and their association with health outcomes of patients with knee osteoarthritis undergoing total knee arthroplasty:

Studies objectively measuring changes in LPA (times spent standing and walking) and SB (time spent sitting) in patients with knee OA undergoing TKA are lacking in a low-middle income knee OA population. Associations between changes in times spent sitting, standing and walking and improvements in PROMs in knee OA patients following TKA are lacking. The third objective was to measure changes in times spent sitting, standing and walking from preoperative to six months postoperatively using an activPAL accelerometer. I also aimed to examine the association between changes in PROMs and objectively measured times spent sitting, standing and walking as well as step counts at six months postoperatively. The first hypothesis was that there would be changes in the low intensity activities at six months after TKA. The second hypothesis was that there would be association between the changes in PROMs and changes in objectively measured low intensity activities.

Figure 1.4 below shows the conceptual framework of the thesis.

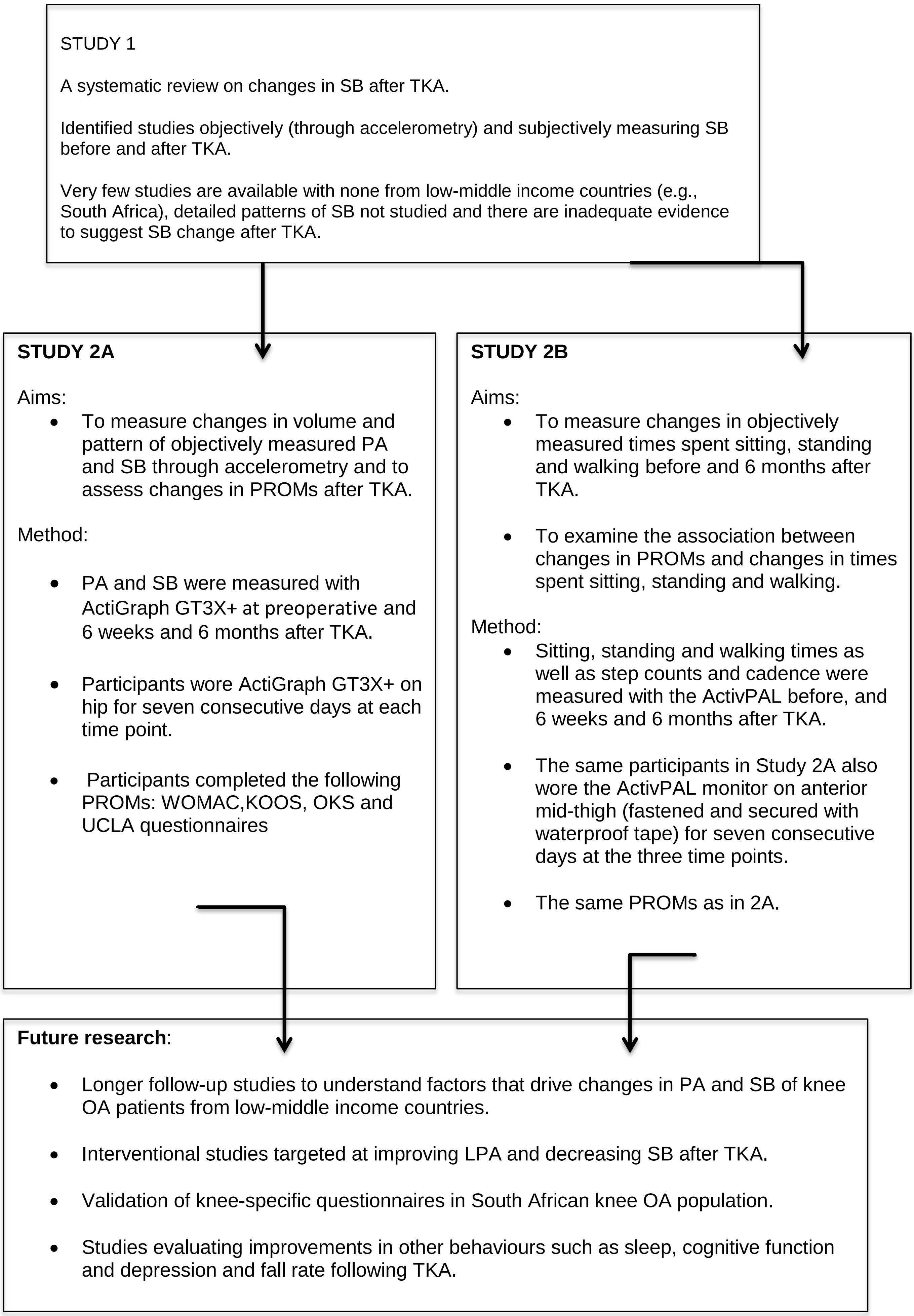

Figure 1.4 A flow chart showing the conceptual framework of the thesis.

TKA: total knee arthroplasty; UCLA: University of California Los Angeles Activity Index; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Outcome Scores; KOOS: Knee Injury and Osteoarthritis Outcome Scores; OKS: Oxford Knee Score; PROMs: patient-reported outcome measures.

CHAPTER 2 – SYSTEMATIC REVIEW

SEDENTARY BEHAVIOUR IN PATIENTS WITH KNEE OSTEOARTHRITIS BEFORE AND AFTER TOTAL KNEE ARTHROPLASTY: A SYSTEMATIC REVIEW[1]

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[1] Frimpong E, McVeigh JA, Meiring RM. 2017. Sedentary behaviour in patients with knee osteoarthritis before and after total knee arthroplasty: A systematic review. *J Aging Phys Act.2017, 18:1-38.doi: 10.1123/japa.2017-0214.*

2.1 Introduction

Osteoarthritis (OA) is a major cause of pain and functional limitation in older adults (89,90). End-stage OA is characterised by severe joint space narrowing, decreased range of motion (ROM), crepitus on motion, osteophyte formation and subchondral bone sclerosis (3,91). Knee OA is the most common form of osteoarthritis accounting for 41% of limb arthritis (11). Patients with knee OA also have severe knee pain (15,17), decreased physical activity (PA) (39,284,285) with increased sedentary behaviour (SB) (286), decreased functional capacity and poor quality of life (41,107).

The most cost-effective treatment for advanced knee OA is total knee arthroplasty (TKA) (27,28). Total knee arthroplasty is considered as a treatment option after all conservative treatment measures have been exhausted, and usually if pain persists for at least six months (27,28,37). The objectives of TKA are pain relief, improvements in quality of life and physical functions (including an increase in habitual PA and a decrease in the time spent sedentary) (29,30,111,112).

Sedentary behaviour is defined as any waking behaviour characterised by an energy expenditure below 1.5 metabolic equivalents (MET) while in a sitting or reclined posture (159). Sedentary behaviour can be measured subjectively (using self-report questionnaires)and objectively (with activity monitors such as accelerometers or posture monitors) (48). Many studies have used self-report measures to assess time spent sedentary such as television viewing time as a proxy measure of overall SB (176,189). Although, self-report measures are easy to administer, readily accessible and inexpensive, they have poor validity and reliability and biased regarding recall (48,49,148,189). However, accelerometers are an objective and reliable means for measuring time spent sedentary and ambulatory activity (287,288). The advent of physical activity monitors to objectively assess combinations of movement behaviours (sedentary, light, moderate and vigorous physical activities) has enabled the important associations between these combinations and health outcomes (52) to be better studied.

Previous systematic reviews and/or meta-analyses have focused only on whether changes in PA (54,55,284,289) and/or return to sports (290) occurs following TKA. A review by Arnold et al (54) summarized objectively measured PA after both total hip arthroplasty (THA) and TKA and concluded that negligible changes in PA occur following TKA. Furthermore, a recent systematic review and meta-analysis also synthesized changes in PA only relative to pain, quality of life and physical function following THA and TKA and also concluded that no change in PA occurs at six months but a small to moderate change occurred at 12 months post-operatively (55). The failure of PA levels to improve post-TKA suggests that patients remain sedentary post-operatively regardless of surgical success (40,42,291). Although the studies reviewed in the above-mentioned systematic reviews used measures of activity behaviour none of them primarily indicated SB assessment as part of the study objectives.

Therefore, following TKA, little attention has been paid to SB, which accounts for the majority (39%) of our waking time (70). Public health and clinical guidelines for managing knee OA recommend regular low-impact PA, as the use of PA guidelines (150 mins/wk of MVPA for healthy adults) may be too high a criterion for older adults with chronic conditions to attain (40,118,292,293). Therefore a reduction in SB (and a corresponding increase in light physical activity- LPA) may be a more realistic target for patients following TKA.

Despite evidence suggesting that there are negligible changes in PA following TKA there is no clear understanding as to whether SB improves following TKA. Therefore, the objective of this systematic review is to integrate the available evidence on changes in SB in patients with knee OA after TKA.

2.2 Methods

2.2.1 General method and registration

The review protocol has been registered with the International Prospective Register for Systematic Reviews (PROSPERO) with registration number: PROSPERO 2017: CRD42017059010 and it is available at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017059010. This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (294).

2.2.2 Search strategy

This systematic review was conducted on published studies in English language from January, 2002 to 31st October, 2017. A comprehensive systematic search of the literature was carried out using the following electronic databases: PUBMED, MEDLINE, CINAHL, COCHRANE, SPORTDiscus, Scopus and Google Scholar. The literature search was conducted with medical subject headings (MeSH) and keywords in the title, abstract and text for the population, intervention, comparator and outcomes (PICO). The keywords and MeSH terms that were used in the search strategy included: “sedentary behaviour” OR “objectively measure sedentary behaviour” OR “subjectively measured sedentary behaviour” OR “physical activity” OR “objectively measured physical activity” OR “subjectively measured physical activity” OR “osteoarthritis” AND “physical activity” OR “osteoarthritis” AND “sedentary behaviour” OR “total knee arthroplasty” AND “physical activity” OR “total knee arthroplasty” AND “sedentary behaviour” OR “accelerometers” OR “light physical activity” OR “moderate physical activity” OR “vigorous physical activity” OR “step counts”. Two investigators (EF, RMM) independently searched the databases for consistency of search hits. In addition, the reference lists of all included articles were searched for relevant studies that were not captured by the original search strategy.

2.2.3 Eligibility criteria (inclusion and exclusion criteria)

Studies were included in the review if they: (a) were longitudinal or cross-sectional (involving different pre-operative and post-operative participants) studies, using accelerometers (uniaxial, biaxial or triaxial accelerometers) to measure changes in patterns, durations and volumes of SB and PA as well as breaks in SB of knee OA patients before and following TKA with varied follow-up times or (b) measured SB and/or PA using self-report measures or questionnaires or (c) included adult participants diagnosed with knee OA, undergoing primary single or bilateral TKA and ambulant with or without assistive devices before and after TKA or (d) were conducted in hospital-based and/or free-living or community-based settings. Studies were excluded from the review if they: (a) measured PA with pedometers or (b) reported on self-report or perceived functional performance and/or functional capacities without measures of SB and/or PA or (c) were interventional trials assessing impacts on SB and PA with either pharmacological agents or non-pharmacological modalities such as structured exercise programmes without a standard care control or (d) involved participants diagnosed with hip OA or rheumatoid arthritis (RA), scheduled for or had undergone THA, partial knee arthroplasty (PKA) or unicondylar knee arthroplasty (UKA), had conditions which limit PA such as stroke and lower limb fractures or were using assistive devices for conditions other than knee OA before and after TKA.

2.2.4 Selection of relevant studies

Two reviewers (EF, RMM) screened titles and abstracts of all retrieved literatures for inclusion based on the eligibility criteria. Any disagreements were resolved by discussion to achieve consensus for a review of full-text articles. The two independent reviewers removed duplicates of databases searched.

2.2.5 Data extraction

Two reviewers (EM, RMM) agreed on which set of data to extract from the included articles. Data extraction from the included articles were performed with a predetermined data extraction sheet by one reviewer (EM) and cross-checked for accuracy and consensus by a second reviewer (RMM). For each included article, data regarding authorship (names, affiliations and country), year of publication, study design with assessment time points pre- and post-operatively, objective and/or subjective outcome measures of SB, characteristics of participants (sample size, age, BMI, gender distribution, side of TKA, type of implants and comorbidities), type of accelerometers, conflict of interest (COI) including funding sources and study findings were extracted, summarised and presented appropriately in tables.

2.2.6 Critical appraisal of methodological quality

The Scottish Intercollegiate Guidelines Network (SIGN) Methodology Checklist 3: Cohort Studies (295) was used to assess the methodological quality of the included articles. This tool is primarily a 15-item checklist assessing methodological designs in two sections: internal validity (comprising 14 items) and overall assessment of methodological quality of the study (1 item). The section one of this tool is further subdivided into subsections including: appropriate and clearly focused study question (1 item), selection of subjects (five items), assessment (6 items), confounding (1 item) and statistical analysis (1 item). Response to each of the items is either *yes*, *no*, *can't say* or *not applicable*. In addition, it requires the recording of drop-out rate (as a percentage). The overall methodological quality was coded as follows: High Quality (++), Acceptable Quality (+) and Low Quality (0). Furthermore, retrospective, single cohort and studies that do not report on more than one or two of the questions attracted low ratings (295). Two independent reviewers (EF, RMM) assessed the risk of bias of the included studies. Agreement on ratings was reached by discussions between the two reviewers.

2.2.7 Data synthesis

Data for pre-operative and post-operative assessment time points were collected and tabulated. Means, standard deviations, medians, inter-quartile ranges, confidence intervals and p-values were extracted from the included studies. The synthesis of findings of included studies was done by a non-quantitative or narrative approach.

2.3 Results

2.3.1 Study identification

A total of 4,868 studies were obtained from the initial electronic databases search. Ten (10) studies were included in the final review after applying the eligibility criteria (Table 1). The details of the process of study identification and selection in accordance with the PRISMA statement (294) are presented in FIGURE 2.1.

2.3.2 Study characteristics

Table 2.1 summarises the characteristics of the 10 included studies. The studies were published between 2002 and 2017 with nine of the studies published between 2010 and 2017 (40,42,44,53,59,64,68,146,280) and one in 2008 (39). The included studies were conducted in five countries namely: Germany (n=3) (53,64,68), The Netherlands (n=3) (39,42,146), Australia (n=2) (40,280), USA (n=1) (44) and Canada (n=1) (59). Eight of the studies were longitudinal observational designs (39,40,42,44,53,64,68,146) lasting between six months and four years with five studies (39,40,44,64,146) reporting the duration of data collections. The other two studies (59,280) were cross-sectional design assessing activity of pre-operative and post-TKA patients. The duration from pre-operative assessments ranged from four to 58 days and four studies (42,44,59,280) did not report on the time frame from pre-operative assessment to TKA. The follow-up periods ranged from 6 weeks to 48 months (four years). Follow-up assessment was conducted four times in one study (146,280), three times in one study (53), twice in three studies (39,42,44) and once in four studies (40,59,64,68).

Activity was measured objectively in nine studies (39,40,42,53,59,64,68,146,280) and subjectively in one study (44). One study (59) used both objective and subjective measures to describe SB. The objective measurements involved the use of accelerometers including: Dynaport Activity Monitor (53), Activity Monitor (AM) (39), ActiGraph GT1M (40), activPAL™ Activity Monitor (64,68), Vitaport Activity Monitor (42), Intelligent Device for Energy Expenditure and Activity (IDEEA) (280), tri-axial accelerometer (activity monitor) (146) and tri-axial ActiGraph GT3X+ (59). The number of valid days in which participants wore accelerometers ranged from one to seven days. The mean wear times of accelerometers per day ranged between 8 and 24 hours. The subjective measurements (using questionnaires) included the University of California Los Angeles (UCLA) Activity Index (44) (which was sub-classified into sedentary (1-2), mildly active (3-4), moderately active (5-7), and highly active (8-10)), Longitudinal Ageing Study Amsterdam (LASA) sedentary behaviour questionnaire (59) and Sedentary and Light Intensity Physical Activity (SLIPA) questionnaire (59).

2.3.3 Clinical characteristics of participants

Table 2.1 also shows the clinical characteristics of participants of the included studies. A total of 1,028 participants were involved in the 10 studies. The sample sizes of studies ranged from 21 to 412. The mean age of participants ranged from 49 to 69 years. The mean BMI of participants of the studies was between 28.5 and 34.4 kg/m^2, and two studies involved participants who were overweight (42,146) while the participants of the remaining studies were obese. There were more females than males in the studies (39,44,53,59,68,280) that reported on gender distributions separately, except in two studies (64,146) which reported more males than females. One study reported data on age, BMI and gender for both TKA and total hip arthroplasty (THA) patients (42). Two studies (39,280) reported on the side of TKA with more right TKAs compared to left. Seven of the studies described the type of implant utilised in the surgeries (39,40,44,53,64,146,280). Furthermore, four studies assessed the co-morbidities of participants (40,64,68,146).

2.3.4 Sedentary behaviour changes after TKA

Table 2.1 shows aspects of SB of participants of the included studies. All the included studies reported on activity behaviours, including SB. However, only one study (59), indicated assessing SB as part of study objectives. The measures used to describe SB across the studies included: “resting time” (53), sit-to-stand (STS) movements (39,146) (number STS per day), times spent sitting and lying/reclining (42,64,68,280), prevalence of sedentary behaviour (44,68), time spent sedentary (40,59) (percentage of accelerometer wear time and actual time) and number of sedentary bouts (59). At the post-operative time points, seven out of the 10 included studies (39,40,59,64,68,146,280) reported no changes in SB measures while the other three studies (42,44,53) reported changes. Out of the three studies which reported changes in SB, two reported improvements or decreases in SB (44,53), whereas the other study reported an increase in SB (42) after TKA. In one study, time spent sitting and lying down as a percentage of wear time significantly decreased from pre-operative to six (p=0.013) and 12 (p=0.003) months post-operatively (53). Another study found that, the proportion of participants who were sedentary decreased at 31-36 months after TKA (44). However, in the other study, mean time spent lying down as a percentage of 24 hours increased significantly (p=0.019) four years after TKA (42). For studies which reported no changes in SB, there were no changes in the time spent sitting and/or lying/reclining at six weeks to 12 months after TKA (64,68,280) and the time spent sedentary did not change at six months (40) and 12 months (59) after TKA, as did the number of sedentary bouts 12 months after TKA (59). Similarly, the number of sit-to-stand (STS) movements (denoting breaks in SB i.e. changes in posture) did not increase significantly (p=0.06) at six months (39) and STS tended to decrease in one study six weeks (146) post-operatively.

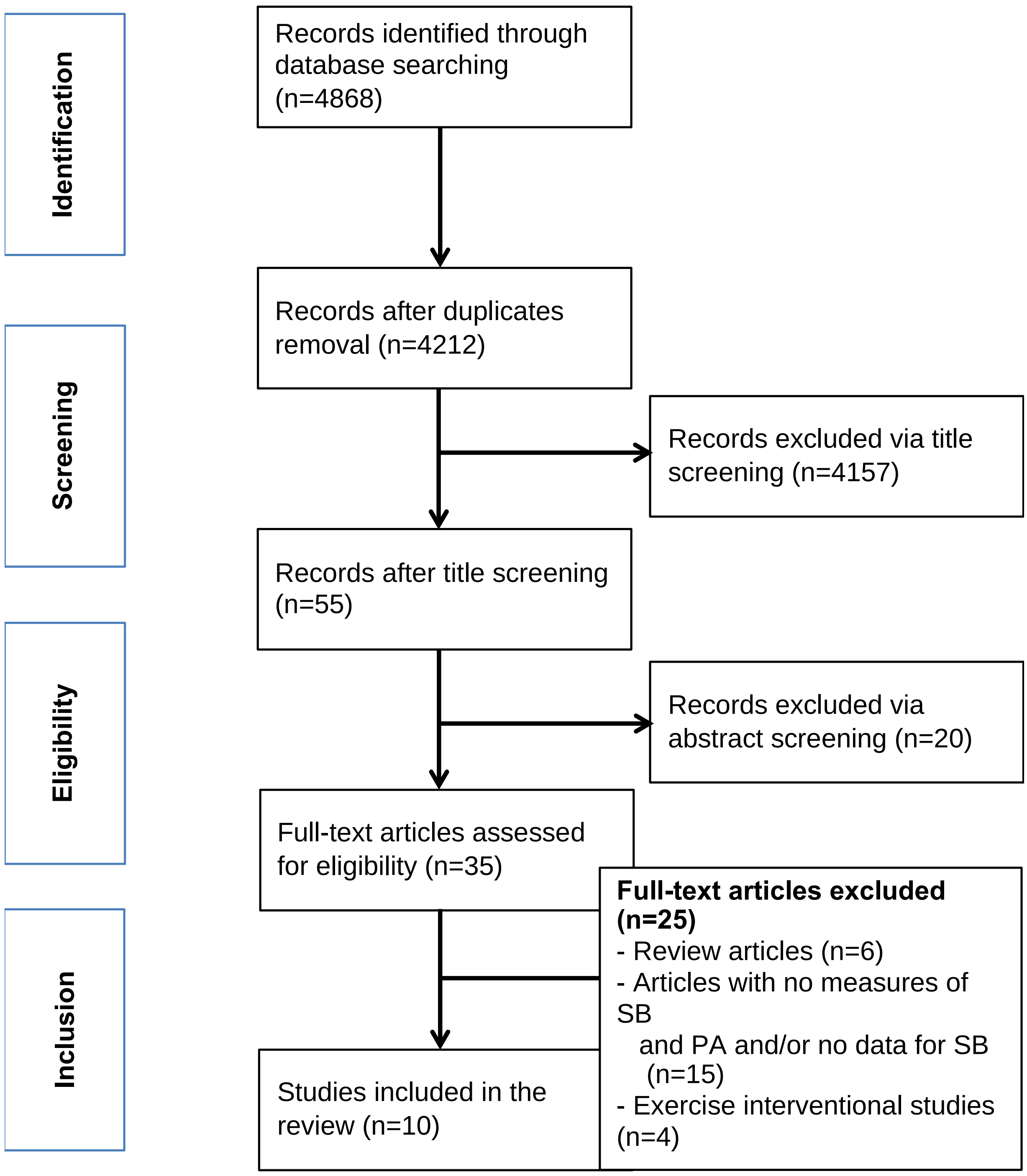

Figure 2. 1 Flow chart of studies identification and inclusion in the systematic review.

SB: sedentary behaviour

Table 2. 1 Summary of studies measuring sedentary behaviour before and after TKA.

Study (Country)	Study Design	Study Participants	Type of TKA/Clinical treatment	Sedentary behaviour outcome measurements	Pre-operative sedentary behaviour assessment date & data	Post-TKA sedentary behaviour assessment date & data	Main findings
Brandes et al., 2011 (Germany)	Longitudinal	- n: 53 - Sex: (F/M)- 34/19 - Mean age (years): 65.8 (SD: 5.8) - Mean BMI (kg/m^2): 30.7 (SD: 4.1) - Side of TKA: (L/R)- NR - Co-morbidities: NR	- Cementation &Uncementation/Mobile-bearing implant (INNEX CR; Zimmer) &NaviTrack (ORTHOsoft) - Post-operative rehabilitation (first two months after surgery)	- Objective measurement: - DynaPort Activity Monitor (McRoberts) - Valid days worn: 1 day - Mean wear time: 12.3 (SD: 1.8) hours/day	- *21 days to TKA:* *Mean "Resting" (sitting and lying) time, % wear time: 66.2 (SD: 13.2)	- *2 months:* 61.5 (SD: 14.6) - *6 months:* 56.5 (SD: 13.6), *p*=0.013 - *12 months*: 55.7 (SD: 14.6), *p*=0.003	Time spent in sedentary activities decreased significantly
De Groot et al., 2008 (The Netherlands)	Longitudinal April 2004 – May 2006	- n: 44 - Sex: (F/M)- 24/20 - Mean age (years): 62.1 (SD: 9.7) - Mean BMI (kg/m^2): 32.1 (SD: 5.3) - Side of TKA: (L/R)- 20/24	- Computer navigation (Brainlab, Feldkirchen, Germany)	- Objective measurement: - Activity monitor (AM) - Valid days worn: 2 days - Mean wear time: 24 hours	- *43 days to TKA:* *Mean STS Movements, number/24h: 46.2 (SD: 13.7)	- *3 months:* 48.7 (SD: 14.6), *p*=0.28 - *6 months:* 51.0 (15.7), *p*=0.06	No increase in STS movements

		- Co-morbidities: NR					
Harding et al., 2014(Australia)	Longitudinal March 1 – Oct 15, 2011	- n: 25 - Sex: NR - Mean age (years): 69.0 (SD: 8.4) - Mean BMI (kg/m^2): 32.0 (SD: 5.5) - Side of TKA: (L/R)- NR - Co-morbidities: Cardiovascular, Diabetes, Respiratory, Musculoskeletal	- GENESISTM II (Smith & Nephew Inc, Memphis, TN, USA) or Stryker ® Triathlon (Stryker Orthopaedics) - Post-operative rehabilitation: standard physiotherapy from day one after surgery. 61% of participants discharged home with out-patient physiotherapy and the remaining discharged to local in-patient rehabilitation centres.	- Objective measurement: - UnixialActiGraph GT1M (ActiGraph LLC, Fort Walton Beach, FL, USA) - Valid days worn: 7 day - Mean wear time: 14 hours	- 58 *days to TKA:* *Median time engaged in sedentary activity, % total time: 82 (IQR: 7.1)	- *6 months:* 83 (7.9), *p*=0.17	No change in time spent in sedentary activities
Hayes et al., 2010 (Australia)	Cross-sectional	- n: 65 - Sex (F/M): Pre-TKA:	- Posterior stabilized fixed bearing	- Objective measurement:	- *Days to TKA- NR:* *Sitting, % waking time:	- *1.5, 3, 6 & 12 months:* - no significant	Times spent sitting

		7/6; post-TKA: 32/24 - Mean age (years): Pre-TKA- 61.1 SD: 2.2); post-TKA- 62.2 (SD: 3.4) - Mean BMI (kg/m^2): Pre-TKA- 30.3 (SD: 2.8); post-TKA- 29.6 (SD: 8.9) - Side of TKA (L/R): pre-TKA- 4/9; post-TKA- 22/31	prosthesis (Genesis II, Smith &Nephew, Memphis, Tennessee, USA), cementation of tibia component and uncementation of femeral component. - Post-operative rehabilitation: physiotherapy (first three months after surgery)	- Intelligent Device for Energy Expenditure and Activity (IDEEA) (Minisun, Fresno, USA) - Valid days worn: 1 day - Mean wear time: 24 hears	54.0 *Lying/reclining, % waking time: 8.0	difference in sitting time between pre-operative and post-operative time points (46-52%), *p*=0.918 - no significant difference in lying/reclining time between pre-operative and post-operative time points (8-23%), *p*=0.243	and lying did not change significantly
Keeney et al., 2014 (USA)	Longitudinal January 2000 – December 2009	- n: 412 – younger participants ≤55 years =150 (181 TKAs); older participants ≥65 to75 years =262 (314 TKAs) - Sex (F/M): younger participants: 111/39; older participants: 178/84 - Mean age (years): younger participants	Posterior stabilization, cruciate retraining, medial pivot, constrained condylar	- Subjective measurement: - University of California Los Angeles (UCLA) activity index. - the UCLA activity scale was sub-classified into:	- *Days to TKA- NR:* *Prevalence of sedentary behaviour (%): - younger patients: 87% - Older patients =77%;	- *30.8 months for* younger participants: 56% - *36.1 months for* Older patients =52%	Prevalence of sedentary behaviour decreased

		=49.0 older participants =69.9 - Mean BMI (kg/m^2): younger participants =34.4 older participants =31.5 - Side of TKA (L/R): NR - Co-morbidities: NR		Sedentary (1-2), Mildly active (3-4), Moderately active (5-7), and highly active (8-10)			
Lützner et al., 2016 (Germany)	Longitudinal	- n: 221 - Sex: (F/M)- 126/95 - Mean age (years): 68.1 (SD: 9.5) - Mean BMI (kg/m^2): 31.3 (SD: 4.9) - Side of TKA: (L/R)- NR - Co-morbidities: ASA Grade 3 or 4 = 43.9%	- Type of TKA/clinical treatment NR - Post-operative rehabilitation NR	- Objective measurement: - ActivPAL™ Activity Monitor (PAL Technologies, Glasgow, UK) - Valid days worn: 4 days - Mean wear time: 24 hours	- *7 days to TKA:* * Mean lying time (hours/day): 12.3 (SD: 2.3) *Mean sitting & standing (hours/day): 10.6 (SD: 2.9) *Percentage sedentary n(%): 106 (48.0)	- *12 months:* 12.0 (SD: 2.4), p=0.203 - *12 months:* 10.4 (SD: 2.3), p=0.475 - *12 months:* 77 (34.8)	No change in times spent sitting and lying
Lützner et al., 2014 (Germany)	Longitudinal March 2009-Sept. 2011	- n: 97 - Sex: (F/M)- 45/52 - Mean age (years): 68.9 (CI: 67.2-70.6)	- Cementation/ standard (43%) & high flexion (5.7%)(Scorpio & Scorpio NRG,	- Objective measurement: - ActivPAL™ Activity Monitor (PAL	- *7 days to TKA:* * Mean sitting & standing time (hours/day): 10.8 (SD:	- *12 months:* 10.3 (SD: 2.6), p=0.258	No change in time spent sitting and

		- Mean BMI (kg/m^2): 31.3 (CI: 30.3-32.3) - Side of TKA: (L/R)- NR - Co-morbidities: ASA Grade 1 or 2 (n=50), ASA Grade 3 or 4 (n=47)	Stryker, Mahwah, NJ, USA) - Post-operative rehabilitation NR	Technologies, Glasgow, UK) - Valid days worn: 4 days - Mean wear time: 24 hours	3.7) *Mean lying time (hours/day): 12.2 (SD: 2.4)	*- 12 months:* 12.2 (SD: 2.7), *p*=0.982	lying
Schotanus et al., 2016 (The Netherlands)	Longitudinal April 2014- December 2015	- n: 20 Sex: (F/M)- 7/13 - Mean age (years): 65.5 (SD: 6.1) - Mean BMI (kg/m^2): 28.5 (SD: 5.4) - Side of TKA: (L/R)- NR - Co-morbidities: ASA I/II/III ERP 2/8/0 and OS 3/7/0	- Cementation, Patients Specific Guides (Signature, Zimmer Bioment, Warsaw, IN, USA)/Vanguard CR TKA (Vanguard CR, Zimmer Biomet, Warsaw, IN, USA) - Post-operative mobilizations for both Enhanced Recovery Pathway (ERP) in <6 hours and Outpatient Surgery (OS) in <4 hours after surgery	- Objective measurement: - Triaxial Activity Monitor (GC Dataconcepts LLC, Waveland, USA) - Valid days worn: 4 days - Mean wear time: ≥8 hours/day	*- 4 days to TKA:* * Time spent sitting: NR *Sit-to-stand transitions (number/day): Enhanced Recovery Pathway (ERP) group- 38; Outpatient Surgery (OS) group- 48	*- 6 weeks:* ERP group- 509.3 (66.5%); OS group- 404.4 (68.5%) *- 6 weeks:* ERP group- 26; OS group- 34	Pre-operative sitting time not reported. Number of sit-to-stand movements tended to decrease.

Vissers et al., 2013 (The Netherlands)	Longitudinal	- n: 21 - Sex: NR - Mean age (years): 63.9 (SD: 9.4) - Mean BMI (kg/m^2): 29.7 (5.0) - Side of TKA: (L/R)- NR - Co-morbidities: NR	NR	- Objective measurement: - Activity Monitor (AM) (Rottterdam AM, Vitaport Technology, The Netherlands) - Valid days worn: 2 days - Mean wear time: 24 hours	- *Days to TKA- NR:* *Mean time spent sitting, % 24h: 35.6 (SD: 9.8) *Mean time spent lying, % 24h: 36.5 (SD: 4.7)	- *6 months:* 37.8 (8.7) - *48 months:* 31.6 (SD: 9.2), *p*=0.068 - *6 months:* 37.0 (SD: 7.7) - *48 months:* 44.0 (SD: 8.2), *p*=0.01	Time spent lying increased significantly
Webber et al., 2017 (Canada)	Cross-sectional	- n: 70 – Pre-TKA=32; Post-TKA=38 - Sex (F/M): Pre-TKA: 21/11; post-TKA: 22/16 - Mean age (years): Pre-TKA- 67.9 (SD: 7.3); post-TKA- 69.9 (SD: 5.3) - Mean BMI (kg/m^2): Pre-TKA- 32.7 (SD: 6.7); post-TKA- 30.5 (SD: 6.1) - Side of TKA: NR	NR	- Objective and subjective measurements: - ActiGraph GT3X+ (ActiGraph, Pensacola, FL) - Valid days worn: 7 days - Mean wear time: 13.9 (SD: 1.1) – 14.4 (SD: 1.1) hours/day	- *Days to TKA- NR:* *Mean sedentary time (% awake wear time): 66.9 (SD: 9.0) *Mean sedentary time, hours/day: 9.3 (1.4) *Median number of sedentary bouts ≥30 mins: 3.4 (IQR: 1.9) *Median sedentary time ≥30 mins bouts: 178.8	- *12 months*: - 63.8 (SD: 10.0), *p*=0.18 - 9.2 (SD: 1.4), *p*=0.62 - 3.1 (IQR: 2.0), *p*=0.37 - 151.1 (IQR: 109.3),	Number of bouts and times spent sedentary did not decrease significantly

	- Co-morbidities: NR	- Longitudinal Ageing Study Amsterdam (LASA) sedentary behaviour questionnaire - Sedentary and Light Intensity Physical Activity (SLIPA)	(SD: 116.2) *Mean sedentary time (by SLIPA-SB) hours/day: 7.2 (SD: 2.7) *Mean sedentary time (by LASA), hours/day: 11.2 (SD: 4.1)	*p*=0.39 - 6.3 (SD: 2.4), *p*=0.17 - 9.7 (SD: 3.3), *p*=0.1

SD: Standard Deviation; IQR: Interquartile Range; F: Female; M: Male; NR: Not Reported; L: left; R: right; TKA: Total Knee Arthroplasty; STS: sit-to-stand; OS: outpatient surgery; ERP: Enhanced Recovery Pathway. *Outcome variables.

2.3.5 Risk of methodological bias

Table 2.2 shows the results of the critical appraisal of methodological quality of the included studies. One out of the 10 studies was of high quality (64), which met majority of the criteria and therefore had little risk of bias in the methodological design. However, one study (42) had a high risk of bias (not meeting major criteria such as high attrition rate, not analyzing data with confidence intervals and not accounting for confounders). All the studies had clearly focused questions, eligibility criteria, clearly defined outcomes and reliability of assessments of outcome measures. Three of the studies involved two cohorts of patients undergoing TKA and THA (39,40,42) and one study included a healthy control group (64). All of the studies reported on participation rate whereas three out of the 10 studies reported acceptable level of attrition rate (less than or equal to 20%) (39,64,146). Four studies assessed the outcome measures with the acceptable number of days (at least 4 days for estimating PA) (59,64,68,146). Only one study adequately accounted for confounding factors and included them in the analyses and two studies used confidence intervals as a measure of variance (64,280). Overall, the studies were of acceptable methodological quality.

Table 2. 2 Critical Appraisal of Methodological Quality using the Scottish Intercollegiate Guidelines Network Methodology Checklist 3: Cohort Studies Scores.

SIGN Methodology Checklist 3 Items	**Studies**	**Brandes et al., 2011**	**De Groot et al., 2008**	**Harding et al., 2014**	**Hayes et al., 2010**	**Keeney et al., 2014**	**Lützer et al., 2016**	**Lützer et al., 2014**	**Schotanus et al., 2016**	**Vissers et al., 2013**	**Webber et al., 2017**
Selection of Subjects	1.1 Clearly Focused Question	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	1.2 Groups Comparability	N/A	Y	Y	Y	Y	Y	Y	Y	Y	Y
	1.3 Participation Rate	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	1.4 Participation Bias	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	1.5 Attrition Rate/Bias (%)	12-40%	4%	23%	N/A	N/A	26.6%	20%	0	42%	N/A
	1.6 Comparison of Full & Partial Participants	Y	N	Y	Y	Y	N	N	N/A	Y	Y
Assessment	1.7 Clearly Defined Outcomes	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	1.8 Blind Assessment	N/A	N/A	N/A	N	N/A	N/A	N/A	N	N/A	N/A
	1.9 Comparison of Process Measures	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	1.10 Reliability of assessment of measures	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	1.11 Validity & Reliability of Outcome Measures	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	1.12 More than one assessment of prognostic factor	Y	N	N	Y	N	N	N	Y	N	N
Confounding		N	N	Y	N	N	Y	Y	N	N	N
Statistical Analysis with CI		N	N	N	Y	N	N	Y	N	N	N
Overall Quality of Study		+	+	+	+	+	+	++	+	0	+

Y: yes - criteria met; N: no - criteria not met; N/A: not applicable; 0: low quality, most of criteria not met (high risk of bias); +: acceptable, most criteria met (low risk of bias); ++: high quality, majority of criteria met (little or no risk of bias); CI: confidence interval.

2.4 Discussion

This systematic review was conducted to determine whether TKA is associated with a reduction in time spent in SB in patients with knee OA. Based on the available evidence, it appears that following TKA, there are no changes in overall SB. Whereas seven out of the 10 included studies (39,40,59,64,68,146,280) reported no changes in SB, two of the studies (44,53) reported improvements or decreases in SB and one study (considered as having a high risk of bias) reporting increased SB (42). While Brandes study (53) and Keeney study (44) reported significant improvements in SB, Vissers and colleagues (42) found increase in SB after TKA. Only one study was specifically designed to measure SB changes in addition to PA after TKA (59). In this review, similar to the findings of previous reviews (54,55,284), which demonstrated little or no changes in overall PA after TKA (although intensities of activities were not specified), SB also does not change post-operatively. It appears that patients who have had TKA remain as sedentary or as active as they were before surgery. Since activity behaviours are considered as a continuum comprising sleep, SB, LPA and moderate to vigorous activity (MVPA) (152,296), there is the need for studies to consider the potential impact of TKA on activity behaviours in the lower intensities (such as SB and LPA). Offsetting or breaking sedentary time up with LPA or purposeful movements during the day is most likely to increase functional ability and quality of life for patients with knee OA and could be a more attainable PA goal in this group.

There are conflicting and inconsistent observations on SB at different follow-up periods. Sedentary behaviour assessed at short term (such as 6 weeks and two or three months) showed no improvements in SB outcomes (39,53,146,280). Sedentary behaviour improved significantly at six and 12 months follow ups (53), but SB increased at four years post-TKA (42). In one study (53), participants spent approximately seven hours of waking wear time being sedentary post-TKA, which is similar to the range of sedentary time (five to ten hours) reported in previous studies (174,267). However, these results should be interpreted with caution given that activity was monitored for only one day (53). Furthermore, studies which measured activity over a week reported high prevalence of SB at six (83%, 11.6 hours per day) (40) and 12 (63.8%, 9.2 hours per day) (59) months after TKA. However, a range of devices (with differing decision rules and cut points for activity intensities) used to measure activity across studies limit comparisons. It would be useful to report how SB changes after TKA from short to long-term follow-ups to better understand the trajectories of SB changes in patients. This could inform when and what targeted interventions may be needed to decrease SB. Additionally, as people age, there is the tendency for physical activity levels regardless of disease activity to decline (259,297), which further underpins the importance of targeted post-operative rehabilitation to restore or maximise functional recovery to a near normal level and improve quality of life of patients.

The patterns by which SB and physical activity are accumulated may provide rich information for health (298), although the total amount of time spent sedentary and in physical activity may not change in patients undergoing TKA. The studies included in this review lacked detailed descriptions of the patterns of SB before and after TKA. In addition to volume of sedentary behaviour, one study reported the number of bouts and time of sedentary bouts lasting for at least 30 minutes (59). Two studies reported on STS movements (denoting breaks or interruptions in SB) (39,146). Additionally, majority of the studies reported the time spent sitting and/or lying/reclining (42,64,68,280). Given that improvements in sedentary and light activity behaviours are more realistic targets for people with OA, there is a need for a detailed description of patterns of the whole activity continuum before and after TKA. This may inform a paradigm shift in both clinical and public health interventions for decreasing SB and improving physical activity, especially light physical activity in patients undergoing TKA. Therefore, health promotion messages should not only target an increase in time spent in MVPA but also decreasing time spent sedentary (299). Expecting patients with TKA to meet the physical activity guidelines of MVPA may not be a realistic goal post-operatively. Nevertheless, inability to meet the physical activity guidelines has been found to be associated with increased risk of mortality (300) and we should therefore find strategies to improve the combinations of movements behaviours for improved health outcomes.

The evidence base of this review is limited by the lack of studies from other populations such as patients from low to middle-income countries (since all of the included studies originated in high-income countries), low to moderate risk of bias, non-uniform follow-up periods for assessments of sedentary behaviour and use of different accelerometers with different algorithms and decision rules for cut points for sedentary behaviour. Measuring activity for less than three days makes the activity estimate less reliable (301). A narrative approach was used to synthesis findings of included studies, a quantitative method was not planned from the outset.

In conclusion, this review shows that sedentary behaviour does not change following TKA. The finding of this review concurs with what has been reported in prior reviews on physical activity changes after TKA, however, the differentiation between different intensities of activity including SB is lacking. Furthermore, the patterns of accumulation of sedentary behaviour by patients with knee OA undergoing TKA have not been studied. Assessing the patterns of sedentary behaviour may reveal subtleties in changes after TKA. Light physical activity of intentional movements during performance of activities of daily living may be most likely to improve and also interrupt sedentary behaviour following TKA. Therefore, encouraging intermittent interruptions in times spent sedentary with intentional light physical activities may improve functional ability and quality of life regardless of age, gender and body mass index. It is important that public health and clinical practice guidelines promote reductions in sedentary behaviour in patients with knee OA before and after TKA. Both pre-operative and post-operative targeted interventions are needed as an adjunct to TKA for decreasing sedentary behaviour and increasing physical activity in patients with knee OA.

CHAPTER 3 – METHODS AND MATERIALS

3.1 Introduction

Following the conclusions from the systematic review that more detailed assessment of activity behaviours of patients with knee OA are needed, this chapter of the thesis outlines and describes the data collection procedures used in the longitudinal study (Study 2A and B).

3.2 Study site

The study was conducted at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), South Africa. The hospital has a 1,088 bed capacity serving patients from across Gauteng and neighbouring provinces. The study participants were recruited from the Division of Orthopaedics in the hospital. This hospital was chosen because: (1) it is a tertiary hospital that runs several specialist clinics including the Orthopaedic Division where TKA among several other surgeries are performed (2) there is a collaboration between the academic staff of the Faculty of Health Sciences of University of the Witwatersrand and the hospital staff for teaching and research which facilitates accessibility to patients and (3) the proximity of the hospital to the Faculty of Health Sciences Campus makes data collection at the hospital much easier.

3.3 Study design

This study is a longitudinal observational design. After participants' recruitment, baseline assessments were done prior to TKA. After the TKA, participants were followed-up and the same assessments done at baseline were repeated at 6 weeks and 6 months post-operatively. Habitual PA and SB were measured using accelerometry at these specific time points (Figure 3.1). In addition to the activity assessments, general health, mobility, FC, ROM, sleep, pain and anthropometric assessments were conducted at each time point on each participant. Participants were instructed to wear ActiGraph GT3X+ and ActivPAL accelerometers for seven days: (1) 2 weeks before the scheduled TKA (baseline), (2) 6 weeks and (3) 6 months post-operatively. These time points corresponded to the required appointments for patients to consult with their surgeons. On the first day participants completed a general health questionnaire (GHQ) after being examined by doctors of the Orthopaedic Division of CMJAH. The doctors were informed about the study design and were given the inclusion and exclusion criteria for recruiting participants. In addition, the GHQ was also used in including eligible and excluding ineligible participants from the study based on the inclusion and exclusion criteria. After the GHQ, participants also completed the disease-specific functional mobility, physical activity, pain and sleep questionnaires. After these the accelerometers were initialised (set up) and placed on participants to monitor activity and sedentary behaviour for seven consecutive days. Patients reported to the Orthopaedic clinic a week after the first contact to be presented to the Orthopaedic Surgical Team for a possible TKA surgery. During this second visit the accelerometers were collected.

Participants were normally admitted for TKA in the second week and if he or she was medically stable the surgery was carried out. However, not all of the participants recruited underwent the surgery. After the surgery, while in hospital, all the patients received in-patient usual physiotherapy care. Upon discharge, participants were given their 6 weeks follow-up appointments. These dates were recorded and participants were reminded via phone calls prior to the appointments. After the 6 week follow-up, the 6 month appointments were also scheduled for each participant and they were again reminded prior to the appointments to facilitate compliance to the assessment time points. The data collection was conducted for a period of 20 months between August 2015 and April 2017.

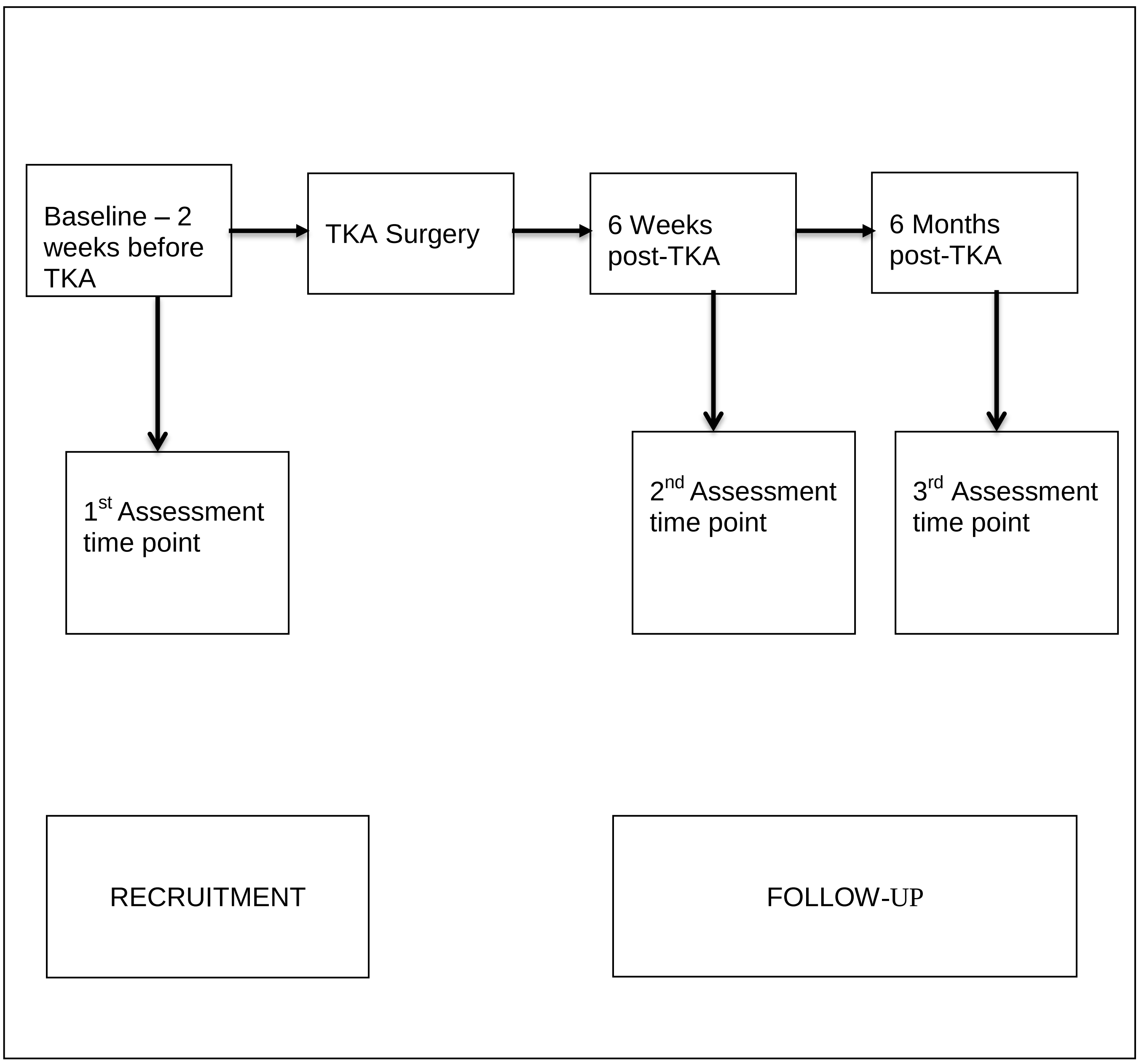

Figure 3. 1 Time points for assessments of habitual physical activity, sedentary behaviour, functional capacity or performance measures, quality of life, general health, mobility, sleep and pain questionnaires.

3.4 Study participants

The study population included all patients with knee osteoarthritis receiving care at the CMJAH. The participants for this study were patients with knee OA scheduled (on surgical waiting list) for a single primary TKA at the CMJAH. The patients were eligible to participate in the study if they were: (1) either males or females between 45 and 85 years of age, diagnosed with knee OA according to the American Rheumatology Association (ACR) criteria for OA and had Kellgren and Lawrence grade 3 or 4 radiographic changes (302) and attended to by surgeons in the Orthopaedic Division at the CMJAH, (2) refractory or unresponsive to analgesics for at least six months, (3) undergoing first-time single (left or right) TKA surgery and (4) ambulant with or without assistive devices. On the other hand, patients were excluded from the study if they were: (1) diagnosed with rheumatoid arthritis (RA) in accordance with the American College of Rheumatology (ACR) criteria (303), (2) scheduled for bilateral TKA or a second knee arthroplasty or revision surgery, (3) scheduled for total hip replacement, (4) to undergo another surgery following the knee arthroplasty, (5) using assistive ambulatory devices for mobility problems other than knee OA or were non-ambulant or wheel chair-bound or (6) having co-morbidities (as diagnosed by a doctor) or medical conditions that affect physical activity such as congestive heart failure, neurological problems (such as stroke and others) and chronic obstructive pulmonary disease (COPD).

3.5 Sample size determination

Based on a previous study that has shown a 17% reduction in average sedentary activity counts in patients with RA before and after therapy (304) an a priori sample size calculation showed that a total sample size of 54 would be required in this study to detect a significant effect of TKA on sedentary activity with a power of 90%. A dropout rate of 20% was expected which brought the calculated minimum sample size to 70.

3.6 General Outcome measures

Table 3.1 shows the outcome measures, their assessment methods and assessment time points. The primary and secondary outcome measures were assessed in each participant at each assessment time point (baseline, 6 weeks and 6 months post-TKA). The primary outcomes were an increase in objectively measured habitual physical activity and a decrease in objectively measured sedentary behaviour. The secondary outcome measures were improvements in osteoarthritis-specific functional and quality of life measures: Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Index, Knee Injury and Osteoarthritis Outcome Scores (KOOS) and Oxford Knee Score (OKS) as well as subjective or self-reported activity using the University of California Los Angeles activity (UCLA) index, pain rating, self-reported sleep quality (305) and objectively measured knee range of motion (ROM).

Table 3. 1 Summary of outcome measures and respective methodology

Outcome		Measurement Method	Time Points (Months)
Primary		**Accelerometry:**	
	Habitual physical activity	ActiGraph GT3X+ (worn on hip) for measuring volume and patterns of LPA, MVPA (number of bouts and bout length or duration) and step counts. ActivPAL monitor (placed and secured on mid-thigh) for measuring walking/stepping and step counts.	0, 6* & 6 post-TKA
	Sedentary behaviour	ActiGraph GT3X+ (worn on hip) for measuring volume and patterns of SB (number of bouts and bout length or bout durations of SB, breaks in SB and sedentary to light ratio: sedentary time divided LPA time). ActivPAL monitor (placed and secured on mid-thigh) for measuring sitting, standing and walking/stepping times.	0, 6* & 6 post-TKA
Secondary			
	Knee ROM	Goniometry	0, 6* & 6 post-TKA
	Quality of life	WOMAC, KOOS	0, 6* & 6 post-TKA
	Pain	VAS	0, 6* & 6 post-TKA
	Sleep quality	Sleep quality questionnaire	0, 6* & 6 post-TKA
	Functional Capacity	WOMAC, KOOS, OKS	0, 6* & 6 post-TKA
	Activity	UCLA Activity Score	0, 6* & 6 post-TKA

LPA: light physical activity, MVPA: moderate and vigorous physical activity; ROM – Range of Motion; WOMAC - Western Ontario and McMaster Universities Osteoarthritis Index; KOOS - Knee injury and Osteoarthritis Outcome Score; TKA – Total Knee Arthroplasty; VAS – Visual Analogue Scale; OKS – Oxford Knee Score; UCLA – University of California Los Angeles Activity Score. 0: baseline or before TKA; *indicates 6 weeks after TKA.

3.7 Ethics

Ethical approval was obtained from the Human Research Ethics Committee (HREC) of the University of the Witwatersrand (ethics clearance number: M150323 -Appendix I). Patients were recruited prospectively, initially through being given an information sheet describing the study and they having the study verbally explained to them at the Orthopaedic Division of CMJAH (Appendix A). Patients who agreed to participate in the study signed a consent form (Appendix B) after having understood the purpose, design and their roles as participants throughout the study period. Participants who could read and write in English gave their direct personal consents but those who were unable to read and write had their relatives give consents on their behalf after explaining the study description in their indigenous languages. Patients were duly informed that they reserved their right to withdraw from the study at any point in time of the study. Although answering the study questionnaires appeared laborious, patients were encouraged to respond to all the questions. To compensate for their transportation, each patient was paid an amount of R 75.00 as transportation cost at anytime they returned the activity monitors to the clinic or the exercise lab.

3.8 Assessments of outcome measures

Data collection was carried out at baseline (2 weeks before TKA), 6 weeks and 6 months after TKA when patients came to the hospital for their mandatory consultations with their surgeons. All of the outcome measures were utilised at each of the assessment time points.

3.8.1 General health questionnaire (GHQ) and socioeconomic status (SES)

A general health questionnaire (GHQ) was used to determine eligibility for the study. The questionnaire gathered information on the overall quality of life in relation to others, health history, history of knee OA, history of medication and smoking, previous or scheduled surgery other than TKA and presence or absence of any co-morbidities (not limited to hypertension, diabetes mellitus, high cholesterol, chronic obstructive pulmonary disorders, heart disease and stroke). Socioeconomic status (SES) was determined using a household amenity questionnaire (HAQ) (306). The GHQ and SES were completed at each visit (Appendix C). The SES has been previously used to assess the socioeconomic status of South Africans (306).

3.8.2 Anthropometric measurements

Height was measured to the nearest metre with the participants shoeless using a stadiometer (Seca, model 202, Germany). Weight was measured to the nearest 0.1 kilograms using a scale (Mettler, Model TE120 ME36400, Switzerland) with the participants shoeless and wearing light clothing. Body mass index (BMI) was calculated from the height and the weight as: [weight (in kilograms) / square of height (in metres)] for each participant at baseline and at the follow-up visits.

3.8.3 Goniometry

Extension and flexion of the affected knee were measured using a plastic goniometer (Protractor Goniometer, Prestige Medical, USA) by an attending orthopaedic surgeon. The knee extension and flexion ROMs were measured using the procedures described by Norkin and White (307). The fulcrum of the goniometer was placed over the lateral epicondyle of the femur. The stationary arm of the goniometer was positioned parallel to the femur with the greater trochanter as a reference point. However, the movable arm of the goniometer was placed along the fibula towards the lateral malleolus. To measure extension, participants were asked to fully extend or straighten the knee, the goniometer was then positioned as described above to record extension. For flexion ROM, participant's knee was put in extension and they were asked to fully flex or bend the knee to an allowable or full ROM with the hip flexed. The goniometer was aligned as described above and flexion ROM recorded.

3.8.4 Functional performance, quality of life and self-report activity assessments

Participants were asked to complete the interviewer-administered osteoarthritis-specific functional mobility questionnaires at each of the assessment time points. The WOMAC, KOOS and the OKS were needed to measure patients' physical function, pain rating and quality of life at different time periods before and after TKA.

3.8.4.1 Western Ontario and McMaster Universities Osteoarthritis (WOMAC)

The WOMAC assesses pain, stiffness and physical function in patients with hip and knee OA*.* The WOMAC consists of 24 items divided into 3 subscales: (1) 5 Pain items for assessing pain (2) 2 Stiffness items and (3) 17 Physical Function or activities of daily living (ADL) items. The previous 48 hours is the time period considered when answering the questions. Each of the items requires the respondent to answer questions on 5-point Likert scale. 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 physical functions or ADL subscales respectively). Higher scores indicate more pain, stiffness and decreased or impaired physical function. Thus, a score of 96 (100%) represents worse possible outcome and 0 represents no impairments or best possible state. The validity and reliability of WOMAC has been previously studied (308–312). Several studies have used WOMAC index following TKA (29,39,313,314) (Appendix E).

3.8.4.2 Knee Injury and Osteoarthritis Outcome Score (KOOS)

The KOOS assesses pain, other symptoms, functions in daily living, sport and recreation (Sport/Rec) and knee-related quality of life (QOL). The KOOS is made up of 42 items grouped into five subdomains: (1) 9 pain items, (2) 7 other symptoms items, (3) 17 functions in daily living, (4) 5 function in sport and recreation items and (5) 4 quality of life items. The previous week is the time period considered when answering the questions. Standardised answer options are given on five (5) Likert scales and each question is assigned a score from 0 (no problems) to 4 (extreme problems). The score is a percentage from 0 to 100, with 0 representing extreme symptoms/problems and 100 representing no problems (315). The validity and reliability of KOOS has been studied in patients with OA and TKA (34,147,316–319). This instrument has been used in previous studies for evaluating outcome after TKA (42,145,313,320,321) (Appendix F).

3.8.4.3 Oxford knee score (OKS)

The OKS consists of 12 questions assessing pain and physical disability using a 5-point Likert scale (0-4). The respondents consider their knee pain and function over the past four weeks when answering the questions. It generates a single score ranging from 0 (worst functional outcome) to 100 (best functional outcome) (322). This clinical tool has been previously validated in TKA studies (186,322,323). The OKS has been used to assess pain and function in studies after TKA (40,314) (Appendix G).

3.8.5 UCLA Activity Index

The University of California, Los Angeles (UCLA) activity index was the subjective physical activity measure used to assess the self-reported activity levels of participants. The UCLA Activity index measures physical activity domain (such as household and leisure-time PA) and activity intensity. The UCLA has items ranging from one to 10, where one is “wholly inactive, dependent on others and cannot leave residence” and 10 means “regularly participates in impact sports” (Appendix H). The participants chose the specific item that best described their physical activity level at each of the assessment time points. The UCLA activity index is simple and easy to answer and does not need any special training before administration. This tool has been found to be one of the best instruments for monitoring activity levels of populations (324). The UCLA activity index has been used in assessing participants undergoing TKA (40,186).

3.9 Measurements of physical activity (PA) and sedentary behaviour (SB)

Habitual PA and SB were objectively measured via accelerometry in each participant at baseline, and six weeks and six months after TKA.

3.9.1 The ActiGraph GT3X+ Accelerometer

The triaxial ActiGraph GT3X+ accelerometer (ActiGraph Inc., Pensacola, FL) was used to measured PA and SB. The ActiGraph GT3X+ is a small (4.6 cm x 3.3 cm x 1.5 cm) lightweight (19 g) tri-axial activity monitor that provides data on PA including activity counts, energy expenditure (kCal), steps and activity intensity (METs) (220). The GT3X+ has an inclinometer to determine body position in sitting, lying and standing and also identifies periods of non-wear and it measures activity in three planes (220). The monitor was attached to an elastic nylon strap that participants wore as a belt around the waist on the side of their hip. For instance, if a participant underwent a left TKA, participants wore the monitor at the waist over the left hip ipsilateral to the left knee (as shown in figure 3.2). In this study, the continuous wear protocol was employed, hence participants wore the ActiGraph for 24 hours/day for seven consecutive days at each of the assessment time points. However, participants were asked to remove the ActiGraph when showering, bathing, swimming or during performing any water-based activities. This was necessary because the ActiGraph is a non-waterproof device. After the seven days of accelerometer wear, the devices were collected from participants and the accelerometry data downloaded.

The ActiGraphs were first initialised (that is, the process of setting up and preparing the accelerometer to collect new data) using its commercial software programme (ActiLife v6, etc). To initialise, the ActiGraph was connected to a computer via USB cable. The process of initialisation involves selecting and in-putting several parameters including: data collection start and end times, collection or sampling rate, participants' identity number (ID), participants' demography (such as gender, date of birth, and race or ethnicity) and anthropometry (including height and weight), side of body to be worn and side of dominance. The ActiGraph could be initialised in advance before starting to record activity and initialisation was only possible when the battery had been charged to 80%. In this study a 30 Hz of sampling rate was used in initialising the ActiGraph throughout the study. After the initialisation, the ActiGraph was mounted on an elastic belt and placed at the respective side of hip. Participants were taught how to put on the ActiGraph in order for them to wear it properly at home after removing the monitor during bathing, swimming or any water-based activities. Emphasis was placed on wearing the monitor on the side of hip corresponding to the knee with TKA. Participants were asked to ensure the black knob covering the USB port always faced vertically upwards. Thus, demonstrations were done for participants to know how to wear the ActiGraph independently.

The raw ActiGraph accelerometry data were downloaded using the commercially available ActiLife software (ActiGraph Inc., Pensacola, FL). The raw data (from the vertical axis) were then epoched into 60 second periods and processed using a custom built SAS algorithm that implemented a series of decision rules with user-modifiable thresholds to automatically identify waking wear data for continuously worn ActiGraph GT3X+ of 60 seconds epoch length (325).

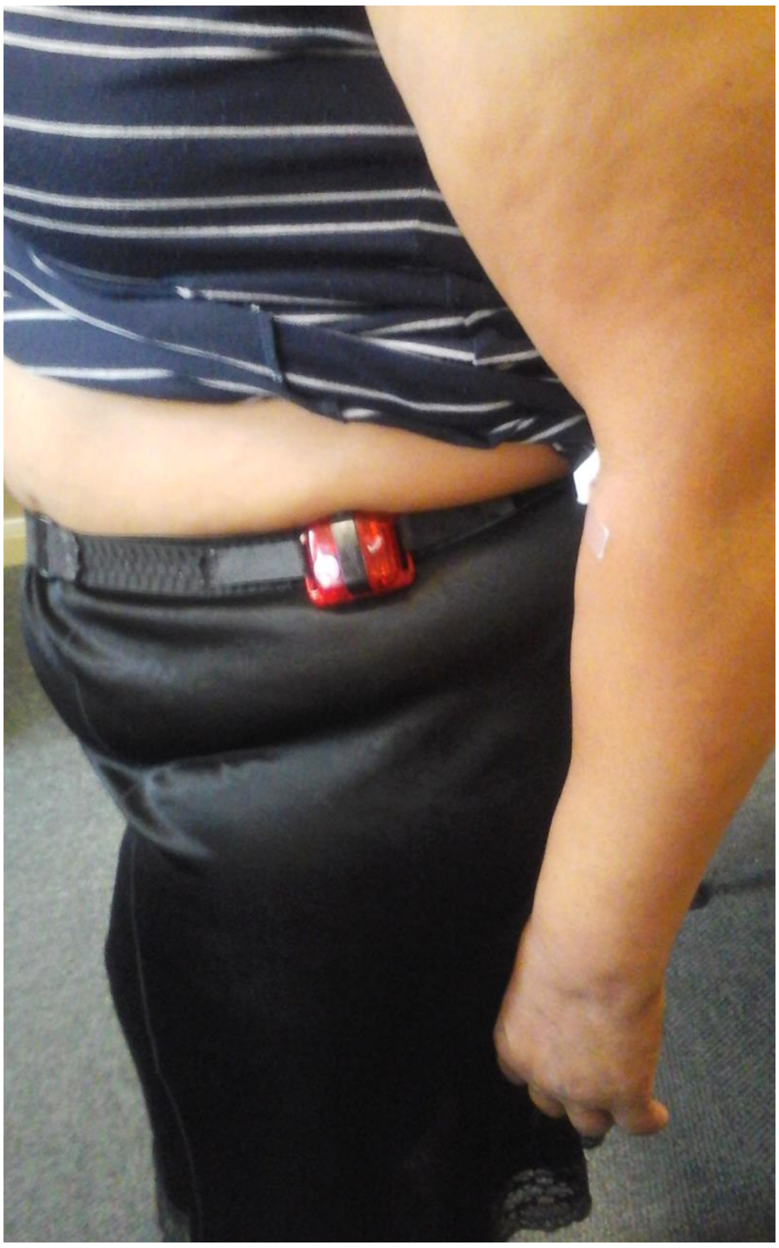

Figure 3. 2 A participant wearing an ActiGraph GT3X+ attached to an elastic strap around the waist over the left hip.

Non-wear and sleep times were removed from the data to obtain the waking wear times. The non-wear time comprises time intervals during which participants do not wear their monitor for prolonged periods for example when participants forget to put on the monitor (208). The non-wear time was classified as one minute intervals with consecutive zero counts for a minimum of 90 minutes (with an allowance of up to 3 minutes of counts between 0 and 50) (326). Similarly, sleep times denote night periods when no recordings or readings are observed from the monitor (208). Different reduction algorithms have been previously described (208,211,326). In the current study, sleep time was removed by both a recently validated algorithm (325) or if valid sleep and wake times could not be detected, participant-reported sleep and wake times were used. A "heat map" generated by the automated SAS algorithm, was generated for each participant and represents the valid activity data that is available for further analysis (as shown in figure 3.3). This heat map was further inspected for quality control purposes.

The wear time forms the basis for estimating proportions of time spent in different activity intensities (327). At least 10 hours of wear time per day were required for a day to be considered valid (174). Only participants with at least four valid days (comprising at least three weekdays and one weekend day) of accelerometer wear (201) were included in the present analyses. Each 60-second epoch of the waking wear data was classified (into sedentary and physical activity intensities) according to cut-points validated for the ActiGraph accelerometer (210). Hence, counts were classified as sedentary if less than 100 counts per minute (cpm) (174), light intensity activity if between 100 and 1951 cpm, moderate-vigorous intensity activity if between 1952 and 5724 cpm and vigorous if greater than 5724 cpm (210). The adjacent epochs within the same intensity were grouped into bouts of the various activities. Total daily time spent in the different PA intensities was obtained by totalling the duration of all of the bouts at each level for each day. The values were then adjusted for wear time and averaged over the number of valid days to derive an estimate of the mean time spent within each activity intensity per day. In addition, the daily patterns of the activities from the morning to evening were also analysed. The total sedentary time measured by the ActiGraph was determined by summing the minutes where counts were less than the cut-point of interest (<100 cpm). The number of breaks in sedentary time was calculated from each period of 100 cpm or less being interrupted by one minute or less of counts greater than 100 cpm. Also, breaks from sedentary time were calculated as instances where a minute identified as sedentary (<100cpm) was followed by a minute identified as not sedentary (≥100 cpm) (225). Finally, the total and mean duration of breaks were also calculated.

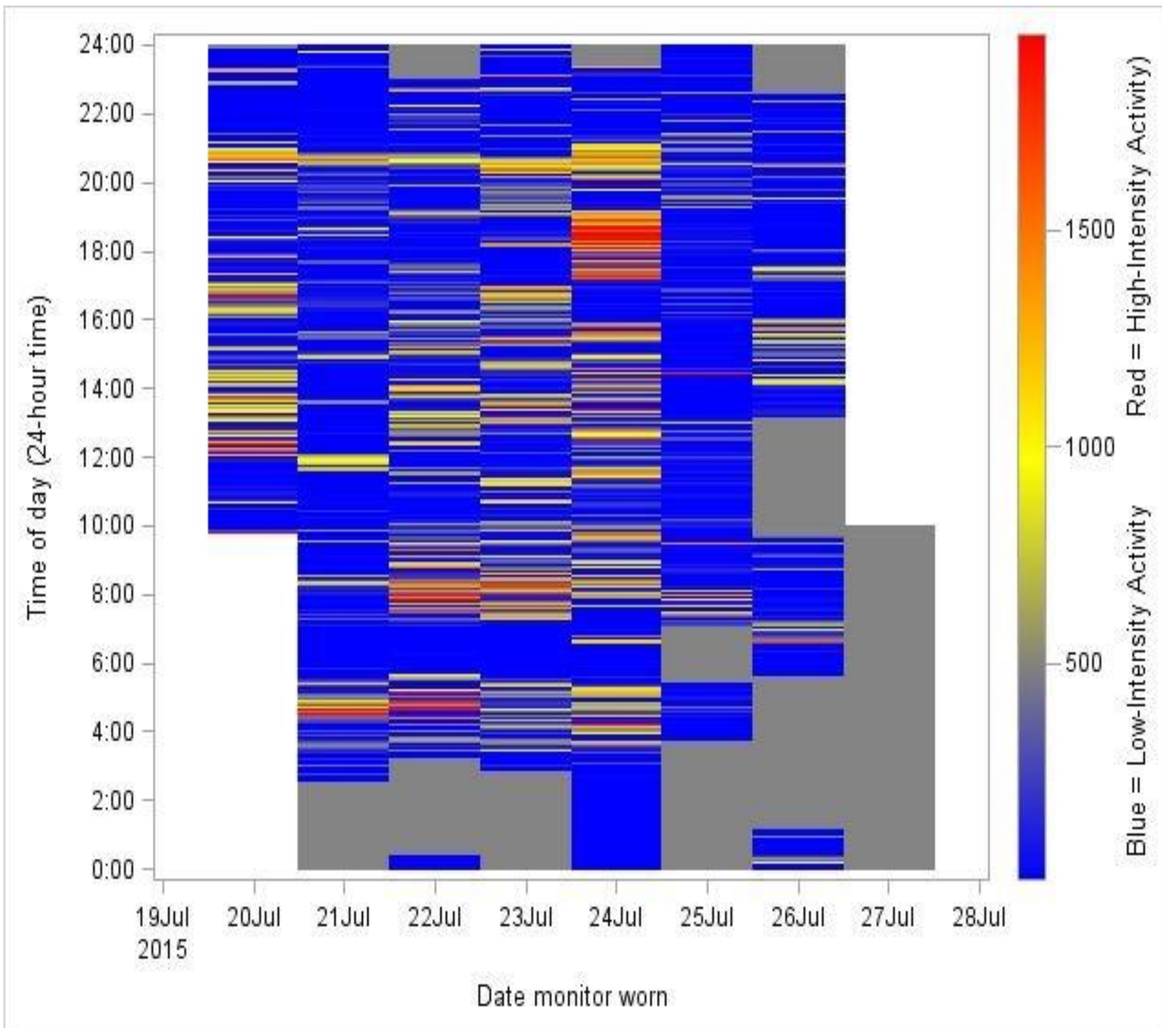

Figure 3. 3 A heat map showing a participant’s activity on days of the week (x axis) and time of day (y axis) from the ActiGraph accelerometer. Grey areas indicate periods of non-wear and sleep; blue: light intensity activity; red: high intensity activity.

3.9.2 *The ActivPAL monitor*

The participants wore a second activity monitor, the ActivPAL (PAL Technologies Ltd, Glasgow, Scotland) to measure times spent sitting, standing and walking as well as step counts and cadence. The ActivPAL is a small (5.1 x 3.6 x 0.8 cm) and light (20.1 g) single-unit device worn on the mid-thigh fastened and secured by a non-allergenic adhesive tape. The ActivPAL uses an inclinometer derived information about thigh position to estimate time spent in different body positions (lying, sitting and standing) in 15 sec epochs (51). Prior to use, the ActivPAL was connected to a computer via a USB cable. The ActivPAL was then set-up for collecting new data using the ActivPAL software (ActivPAL process and presentation, version 7.2.32, PAL Technologies Ltd, Glasgow, Scotland). The sampling rate of the ActivPAL was 20 Hz. After the set-up the ActivPAL was wrapped in a small latex cover and placed on the mid-thigh corresponding to the knee undergoing TKA (as shown in figure 3.4). The ActivPAL was taped to the mid-thigh with a waterproof tape (Hydrofilm®, Hartmann, China). The participants were asked to keep the ActivPAL on for the same amount of time (seven consecutive days) as the ActiGraph GT3X+. Since the ActivPAL monitor was covered with waterproof taping, participants did not need to remove the ActivPAL when showering, bathing or swimming. However, some of the participants noted loss of the adhesiveness of the tape and needed to support the monitor in situ with a normal plaster. The ActivPAL was collected at the same time as the ActiGraph GT3X+ and data downloaded for processing and analyses. After downloading the data, the ActivPAL displays a visual summary (used for quality control) of the week-long activity recordings with yellow, green and red colours denoting sitting/lying, standing and walking or stepping respectively (as shown in figure 3.5).

The ActivPAL data were recorded in 15-sec epochs and the ActivPAL software was used to determine the variables from the downloaded data comprising start time and duration of each sitting, lying, standing and stepping bout (225). Because the ActivPAL was supposed to remain fastened to the thigh for the seven days, there was no need of removing non-wear times unless otherwise participants reported that the device fell off. Sleep periods were either calculated using a validated algorithm (328) or, where distinct sleep times could not be obtained, sleep periods were determined by visual inspection and confirmed from the patient-reported sleep and wake times recorded on the general health questionnaire. (328). The total sedentary time was determined by summing up the duration of all sitting/lying bouts (225). The interruptions or breaks from sedentary time were indicated at points where a sitting/lying bout was followed by a standing or stepping bout (225).

Figure 3. 4 A patient wearing an ActivPAL accelerometer wrapped in latex cover and tapped to the mid-thigh.

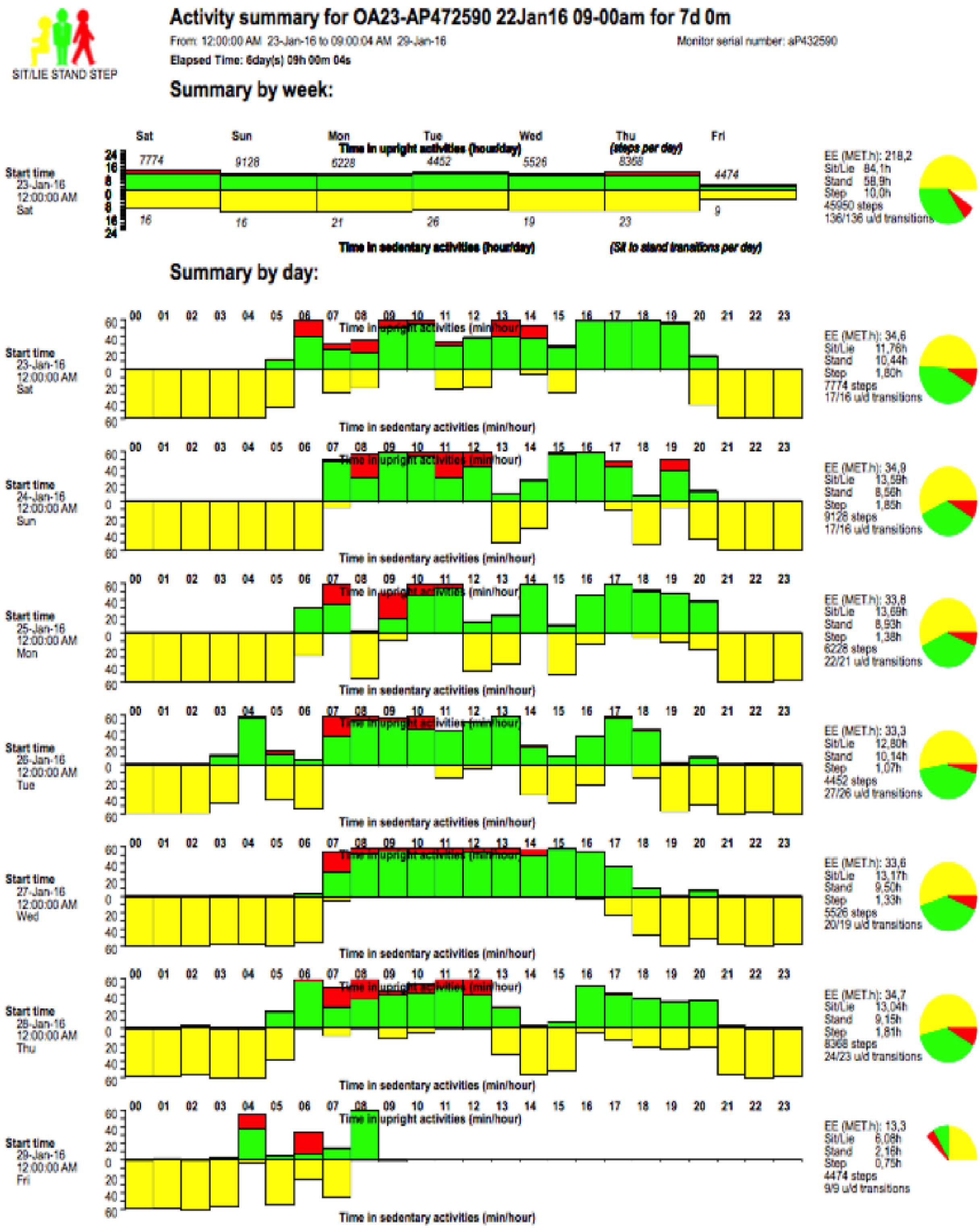

Figure 3. 5 Visual output of a week summary of activity recording by the ActivPAL.

Yellow shows sitting/lying, green, standing, and red, stepping/walking.

3.10 Specific outcome variables for study 2A and study B

Data from the ActiGraph GT3X+ were used for study 2A (Objective 2). The outcome variables included proportions and actual times spent in all activity behaviour intensities (SB, LPA and MVPA) as well as patterns of these activities (numbers and durations of bouts as well as breaks in SB), step counts and the hourly variations of LPA and SB.

Similarly, data from the ActivPAL were used for study 2B (objective 3), including times spent sitting, standing and walking as well as step counts and cadence. In addition to the above stated primary objective measures the PROMs, including WOMAC, KOOS and OKS as well as UCLA activity index described before were used in both studies.

3.11 Data Analysis

3.11.1 Analysis for study 2A

The data were analysed using Statistical Package for Social Sciences (SPSS) (SPSS Inc., Chicago, IL, USA), version 24. All participants with at least four valid days (230) of ActiGraph data at baseline and/or six weeks and six months after TKA were included in the analysis. However, participants' characteristics (anthropometric, general health and socioeconomic data) were reported for all those recruited into the study using descriptive statistics (mean and standard deviation or median and interquartile range or percentages). The amounts of time spent in SB, light physical activity (LPA) and MVPA at baseline and at six weeks and six months after TKA were presented descriptively (using means and 95% confidence intervals or median and interquartile range). SB and LPA data (which were normally distributed, assessed by Shapiro-Wilks test) between baseline and six weeks and six months after TKA were compared using a linear mixed-model whereas a generalized linear model was used for MVPA time and the percentages of awake wear times spent in each of the activity behaviours (not normally distributed). Fixed effect used in the models was time and the random effect was subjects. The variance-covariance structures were selected based on Bayes Information Criterion and the unstructured variance-covariance was used. Participants' age, BMI and awake wear times were included in the models as known covariates. Accumulation of activity across categories of intensity and bout duration was also described using Exposure Variation Analysis (EVA) (329). The hourly variations of the sedentary to light activity ratios were analysed using a generalised linear model with hour of the day and assessment time points as factors.

Scores for UCLA and WOMAC (calculated by the scoring system) were reported descriptively (with median and interquartile range). Questionnaire scores between baseline, six weeks and six months after TKA were compared using a generalized linear model. In all cases where differences occurred between baseline and 6 weeks and 6 months after TKA, post-hoc analyses with Bonferroni's adjustments for multiple comparisons were done. A *p*-value of less than 0.05 was considered significant.

3.11.2 Analysis for study 2B

The same statistical software and valid number of days criteria described for study 2A (section 3.11.1) were also used in study 2B. The percentages of waking wear time and amounts of time spent walking and standing as well as daily step counts and cadence (which were not normally distributed assessed by Shapiro-Wilks test) were log-transformed. Therefore, comparisons of waking wear time, percentages of waking wear times and the actual times spent sitting, standing and walking as well as step counts and cadence between baseline and six weeks and six months after TKA were done using a linear mixed model. Fixed effect used in the models was time and the random effect was subjects. The variance-covariance structures were selected based on Bayes Information Criterion and the unstructured variance-covariance was used. Participants' age, BMI and waking wear time were included in the model as known covariates.

A univariate linear regression was used to determine the association between changes in objectively measured times spent sitting, standing, walking and number of steps, and the change in PROMS (WOMAC, KOOS, OKS and UCLA) adjusting for gender, age, change in BMI and socioeconomic status. The Bonferroni's adjustments for multiple comparisons were done during post-hoc analyses. A p-value of less than 0.05 was considered significant.

CHAPTER 4 – RESULTS

CHANGES IN VOLUME AND PATTERN OF OBJECTIVELY MEASURED PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR FOLLOWING TOTAL KNEE ARTHROPLASTY: A LONGITUDINAL DESIGN[1]

[1] Frimpong E, McVeigh JA, Dick VDJ, Lipalo Mokete, Yusuf KS, Tikly M, Meiring RM. Changes in volume and pattern of objectively measured physical activity and sedentary behaviour following total knee arthroplasty: a longitudinal design. *Knee Surgery, Sports Traumatology, Arthroscopy*, *https://doi.org/10.1007/s00167-018-4987-2*

4.1 Results (Study 2A)

A total of 89 (76 female; 13 male) participants with mean (SD) age of 64.8 (8.7) years ranging from 55-80 years and BMI of 34.0 (7.7) kg/m^2 were recruited into the study. Figure 4.1 is a flow chart showing the total number of participants recruited into the study at baseline and the drop outs to follow up. Only 73 patients underwent the TKA surgery while the remaining 15 participants had their surgeries suspended on account of unsatisfactory clinical reports (n=14) and one participant declined to undergo the surgery due to family issues. A further sixteen participants were lost to follow-up: six dropped out at six weeks post-TKA (three travelled out of Johannesburg, two could not be reached and one opted to continue treatment at a private clinic); and ten dropped out at six months post-TKA (four travelled out of Johannesburg, three declined to continue the study, two lost their monitors and one had a faulty monitor).

TABLE 4.1 shows the participant characteristics for those who (1) underwent TKA surgery; (2) completed the study 6 months after TKA and (3) had valid or insufficient ActiGraph GT3X+ activity data at 6 months after TKA. As shown in table 4.1, patients who completed the 6 months were almost exclusively female and were predominantly Black patients. The commonest co-morbidity was hypertension with over half of the group having hypertension, followed by type II diabetes and dyslipidaemia. Fifty-one percent and 16% of the participants had completed high school and tertiary education respectively. The socioeconomic status (SES) score (approximately, 10 out of 15) was similar among the participants in each category.

Patient and physician-reported outcomes before and after TKA

Self-reported PA was significantly higher at six weeks ($p<0.001$) and 6 months ($p<0.001$) after TKA compared to baseline (Table 4.2). Patients appeared to improve considerably following surgery such that they reported no pain and stiffness 6 months after TKA compared to baseline ($p<0.001$).

Both the flexion and extension ranges of motion (ROM) improved significantly six months after TKA ($p<0.001$ and $p=0.028$, respectively). The range of motion (ROM) of participants improved from baseline (median (interquartile range- IQR): 0.0 - 90.0)° to six months after TKA (median (interquartile range- IQR): 0.0 - 110)° ($p<0.05$).

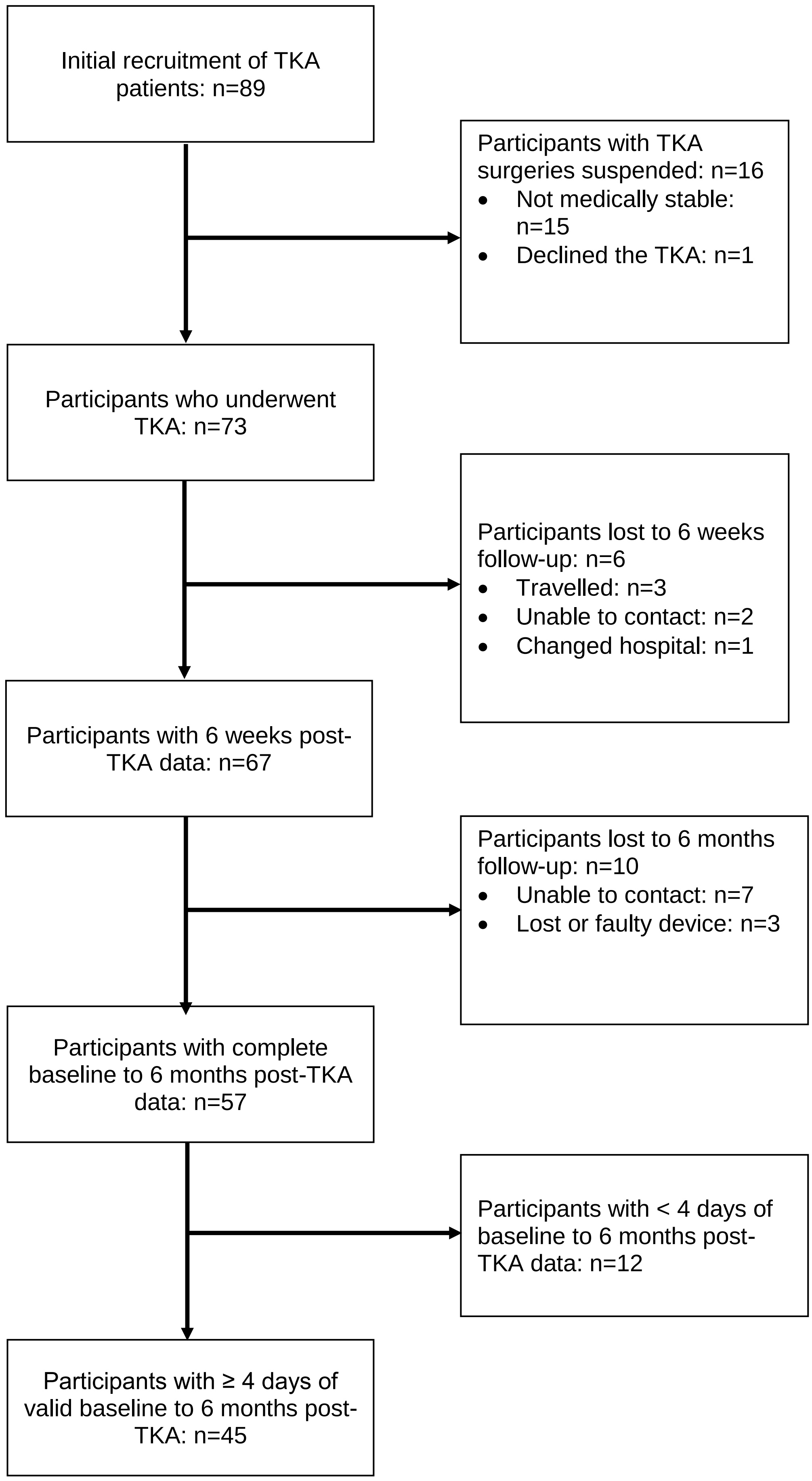

Figure 4. 1 Flow chart illustrating participants' recruitment from baseline to 6 months follow-up

Table 4. 1 Characteristics of participants who underwent TKA, those who completed the follow up and those who completed the follow up with and without valid ActiGraph data

Variables	**Participants who underwent TKA (n=73)**	**Participants with complete 6 months follow-up data (n=57)**	**Participants with complete 6 months and valid ActiGraph data (n=45)**	**Participants with complete 6 months and insufficient ActiGraph data (n=12)**
Age (yrs)	64.0 (8.7)	64.2 (9.0)	63.8 (8.8)	64.3 (9.4)
Gender, n (%)				
Females	67 (92)	53 (93)	42 (93)	12 (100)
Males	6 (8)	4 (7)	3 (7)	0 (0)
Race, n (%)				
Black	53 (73)	41 (72)	33 (73)	11 (92)
Caucasian	20 (27)	16 (28)	12 (27)	1 (8)
Weight (kg)	84.8 (20.0)	84.3 (20.8)	84.6 (21.0)	87.3 (17.5)
Height (m)	1.6 (0.1)	1.6 (0.1)	1.6 (0.1)	1.6 (0.1)
Body mass index (kg/m^2)	34.2 (7.5)	34.3 (7.9)	34.6 (7.8)	36.6 (7.6)
LHS, median (IQR), (days)	7.0 (3)	7.0 (3)	7.0 (3)	7.0 (5.0)
Side of TKA, n (%)				
Left	30 (41)	24 (42)	19 (42)	6 (50)
Right	43 (59)	33 (58)	26 (58)	6 (50)
Smoking (yes), n (%)	6 (8)	4 (7)	3 (7)	3 (7)
Diabetes mellitus (yes), n (%)	8 (11)	5 (9)	5 (11)	1 (8)
Hypertension (yes), n (%)	37 (51)	28 (49)	22 (49)	6 (50)
Dyslipidaemia (yes), n (%)	7 (10)	6 (11)	2 (5)	2 (17)
Educational status, n (%)				
Below high school	24 (33)	20 (35)	18 (40)	4 (33)
High school complete	37 (51)	30 (53)	20 (44)	7 (58)
Tertiary level complete	12 (16)	7 (12)	7 (16)	1 (9)
SES score	9.9 (2.8)	10.0 (2.9)	9.9 (3.1)	9.7 (3.1)

LHS: length of hospital stay; SES: socioeconomic status; TKA: total knee arthroplasty. Age, weight, height, body mass index and SES score are presented as mean (SD); whereas length of hospital stay is presented as median (interquartile range, IQR). The remaining data are presented as frequencies (%). Differences in variables between the groups were not statistically significant (p>0.05).

Table 4. 2 Comparisons of patient and physician-reported outcomes before and after TKA

	Baseline (n=79)	**6 Weeks after TKA (n=62)**	**6 Months after TKA (n=45)**	**Main effect p-value**	**p-value***
UCLA Score	2.0 (1.0)	3.5 (1.0)	5.0 (1.0)	<0.001	<0.001
Total WOMAC score	71.0 (27.0)	22.5 (19.0)	4.0 (11.3)	<0.001	<0.001
Pain	15.0 (6.0)	3.0 (5.0)	0.0 (2.0)	<0.001	<0.001
Stiffness	6.0 (2.0)	2.0 (1.0)	0.0 (2.0)	<0.001	<0.001
ADL	51.0 (17.0)	16.5 (17.0)	3.5 (9.0)	<0.001	<0.001
ROM					
Flexion, (°)	90.0 (10.0)	95.0 (10.0)	110.0 (15.0)	<0.001	<0.001
Extension, (°)	0.0 (6.0)	0.0 (4.0)	0.0 (0.0)	0.01	0.012

Data are presented as median (interquartile range). A higher score for WOMAC pain, stiffness and ADL subscales (maximum scores possible were 20, 8, 68 respectively) indicates a worse outcome. The highest possible score for UCLA is 10, indicating regular participation in impact sports. Normal ROM is 0°-140°, however, ROM of 0°-110° (ie., 0° extension and 110° flexion) after TKA indicates a good result. ***p-value calculated between baseline and 6 months after TKA (Bonferroni).

Changes in volume of activity behaviours pre and postoperatively

Table 4.3 shows the comparisons of total volume and patterns of PA and SB of participants before and after TKA. The number of valid days of ActiGraph wear, total awake wear time per day and total activity counts per day and per minute for all awake wear time were not different between baseline and six weeks and six months after TKA ($p>0.05$).

The percentage of awake wear time spent in SB decreased significantly from baseline to six months after TKA by 6.1% ($p=0.009$). The overall daily sedentary time decreased significantly from baseline to six months after TKA ($p=0.03$) by an average of 55.7 (95% CI: 4.3-107.2) mins/day. The total number of breaks from SB significantly increased at six months after TKA compared to six weeks after TKA ($p<0.001$) and baseline ($p=0.022$). However, the duration of the breaks from SB was not different between baseline and six months after TKA ($p = 0.153$) but was lower at six weeks compared to six months after TKA ($p = 0.013$).

Participants spent more of their awake wear time in LPA at six months after TKA compared to six weeks after TKA ($p=0.001$) and baseline ($p=0.008$). The participants increased their daily LPA time from baseline to 6 months after TKA by approximately 50.0 (95% CI: 3.2 – 96.7) mins/day ($p=0.032$).

The participants spent less than 1% of their awake wear times in MVPA at all time points (Table 4.3). Approximately 5-18% of the participants met the current PA guidelines at baseline and after TKA. Participants' steps per day decreased at six weeks after TKA compared to baseline counts ($p<0.001$), but increased from baseline to six months after TKA by an average of 1265 (95% CI: 199-2330, $p=0.015$) steps/day.

Patterns of accumulation of activity behaviours before and after TKA

Figure 4.2 shows comparisons of the accumulation of participants' awake wear times spent in sedentary, LPA and MVPA intensities accumulated for different bout lengths (EVA) between baseline and six months after TKA. At both baseline and 6 months after TKA, the dominance of sedentary time over other intensities is highlighted in the figure, as is the dominance of short bouts of LPA and MVPA. The percentage of waking wear time spent in LPA bouts lasting for less than 5 mins, 5-9 mins, 10-19 mins, 20-29 mins and 30-59 mins increased significantly from baseline to six months after TKA [(baseline (mean ± SD): (13.7±5.2) vs. 6 months (mean ± SD): 14.5±5.4)%, $p=0.043$; (7.8±3.3 vs. 9.4±3.8)%, $p=0.011$; (5.2±5.9 vs. 6.8±2.8)%, $p=0.017$; (1.5±6.3 vs. 2.4±1.0)%, $p=0.018$ and (0.8±2.0 vs. 0.4±2.1)%, $p=0.002$ respectively)]. Also, the percentages of waking wear time spent in SB of prolonged bout durations of 20-29 min, 30-59 min and of at least 60 min at six months after TKA decreased significantly from baseline [(baseline (mean ± SD): (9.7±2.0) vs. 6 months (mean ± SD): 8.0±2.6)%, $p=0.022$; (14.9±1.8 vs.

12.3±3.3,)% p=0.012 and (11.3±2.0 vs. 7.6±2.3), p=0.033, respectively)]. However the percentages of waking time spent in MVPA bouts lengths did not change significantly from baseline to six months after TKA ($p>0.05$).

Figure 4.3 depicts the hourly variation of awake wear time not spent in MVPA (i.e. the sedentary to light activity ratios) over the course of the day. Overall participants were less sedentary in the early hours of the day (6h00-10h00), after which, time spent sedentary gradually increased through the afternoon to late evening (13h00-23h00). The sedentary to light ratio was similar between baseline and six weeks after TKA, with the exception at 15h00 where the ratio was also different between six weeks and six months post-TKA (p=0.007). However, between baseline and six months after TKA, there was a difference in sedentary to light ratio from morning to early evening with a significant reduction in sedentariness and an increase in light activity from 09h00 to 19h00 ($p<0.05$). There was also a lower sedentary to light ratio at 6 months compared to baseline at 21h00 (p=0.014).

Table 4. 3 Comparisons of volume of activity behaviours before and after total knee arthroplasty

	Baseline (n = 79)	**6 Weeks after TKA (n = 62)**	**6 Months after TKA (n = 45)**	**Main effect p-value**	**p-value***
Valid days	5.7 (5.5-5.9)	6.0 (5.8-6.3)	6.0 (5.7-6.3)	0.067	0.263
Waking wear time (mins/day)	927.0 (903.2-956.7)	901.7 (874.4-929.0)	927.8 (901.7-953.8)	0.126	1.000
Activity counts, all awake wear time (counts/day)	162018 (133675-190361)	132094 (109961-154227)	196751 (165206-228296)	<0.001	0.177
Activity counts, all awake wear time (counts/min)	170 (143-198)	145 (123-168)	209 (177-242)	0.001	0.124
Sedentary behaviour (SB)					
Sedentary time, % awake wear[a]	70.1 (67.5-72.7)	72.0 (69.5-74.9)	64.0 (60.6-67.9)	0.001	0.009
Sedentary time (mins/day)	649.7 (622.0-677.3)	649.1 (617.1-681.1)	594.0 (555.9-632.0)	0.033	0.030
Breaks from SB (number/day)	85.2 (80.4-90.1)	82.2 (76.8-87.6)	93.0 (88.1-97.9)	<0.001	0.022
Duration of break from SB (mins/break)	3.2 (3.0-3.5)	3.0 (2.7-3.3)	3.7 (3.2-4.0)	0.010	0.152
Light physical activity (LPA)					
Light physical activity, % awake wear[a]	29.0 (26.6-31.4)	27.4 (24.7-30.0)	34.8 (31.3-38.3)	0.001	0.008
Light physical activity time (mins/day)	272.8 (247.4-298.2)	245.9 (221.0-279.9)	322.8 (289.0-356.6)	<0.001	0.032
Moderate to vigorous physical activity[a]					
Moderate to vigorous PA, % awake wear	0.1 (0.6)	0.1 (0.5)	0.4 (1.1)	0.266	1.000
Moderate to vigorous PA time (mins/day)	2.0 (7.8)	1.4 (4.9)	3.4 (11.6)	0.292	1.000
Steps (number/day)	3677 (3083-4270)	2816 (2355-3278)	4941 (4109-5773)	<0.001	0.015
Meeting PA guidelines, n (%)[a]	7 (8.9)	3 (4.8)	8 (17.8)	0.054	0.208

All data (adjusted for age, body mass index and waking wear time) are presented as mean (95% CI) except for moderate-vigorous physical activity and ROM (range of motion), which are presented as median (interquartile range). *p-value between baseline and 6 months after TKA (Bonferroni). [a]p-value calculated using generalised linear model; remaining data compared using linear mixed model. Normal ROM is 0°-140°, however, ROM of 0°-110° (ie., 0° extension and 110° flexion) after TKA indicates a good result

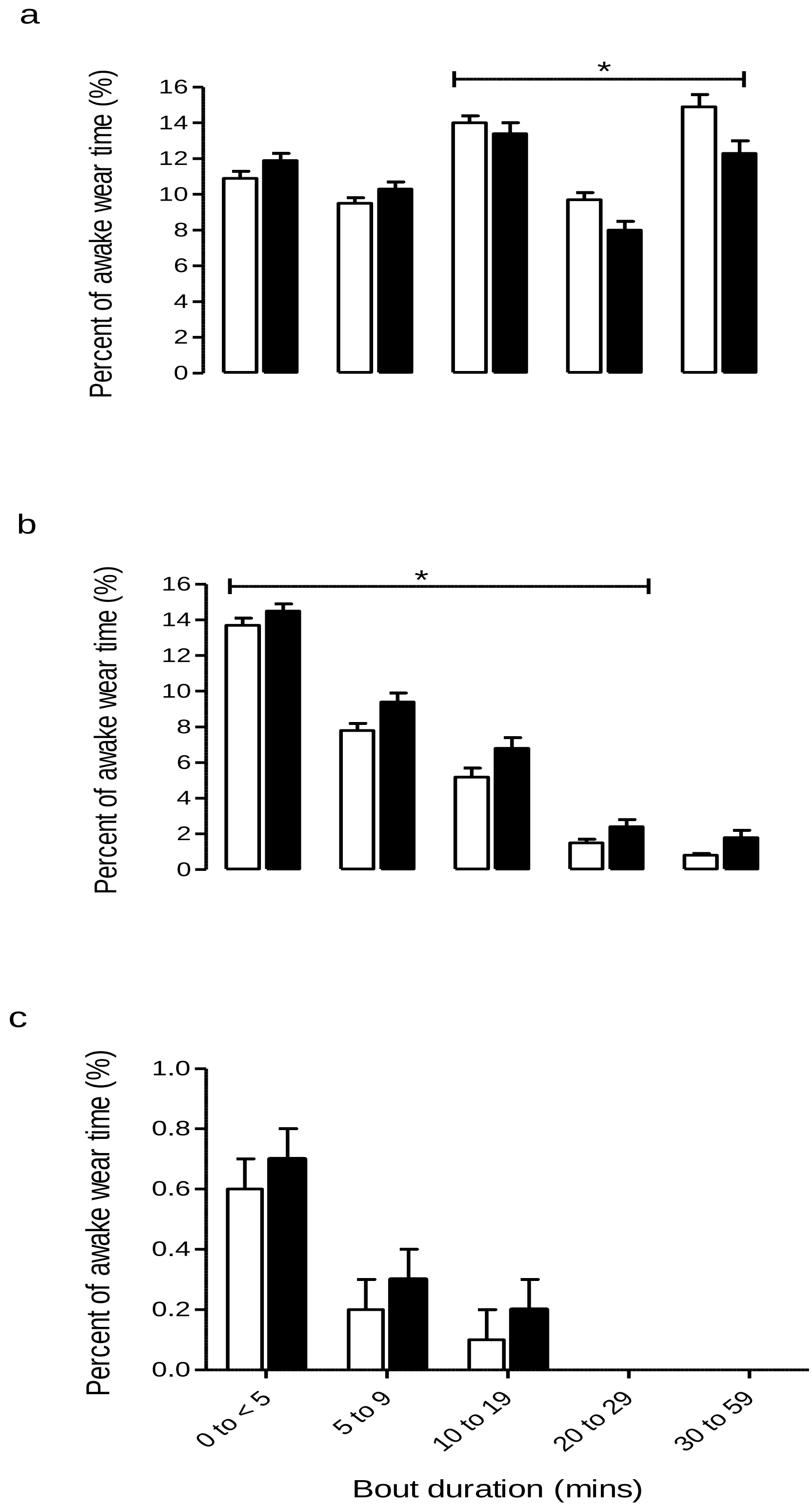

Figure 4. 2 Percent of awake wear time spent in a) sedentary behaviour, b) light physical activity and c) moderate to vigorous physical activity before (white bars) and six months after (black bars) total knee arthroplasty.

*p<0.05 for indicated bouts between baseline and six months after TKA. Data are presented as mean (SEM).

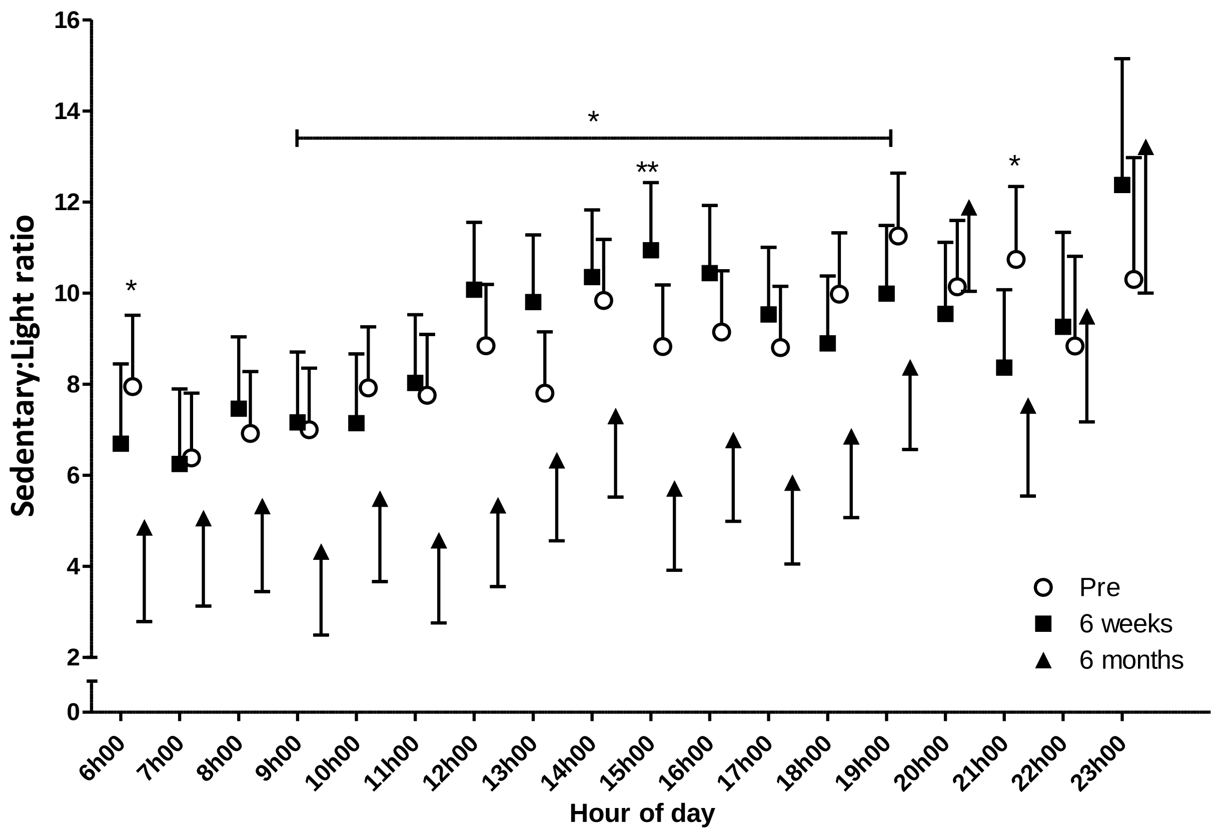

Figure 4. 3 Average hourly sedentary to light activity ratio between baseline and after TKA.

Data are mean (95% CI) sedentary to light ratios per hour of the day for each of the three visits. Data are adjusted for awake wear time. *p<0.05 between pre (●) and 6 months post-TKA (▲).**p<0.01 between 6 weeks (▪) and 6 months post-TKA (▲).

OBJECTIVELY MEASURED CHANGES IN SITTING, STANDING AND WALKING AND THEIR ASSOCIATION WITH HEALTH OUTCOMES OF PATIENTS WITH KNEE OSTEOARTHRITIS UNDERGOING TOTAL KNEE ARTHROPLASTY[1]

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[1] Frimpong E, McVeigh JA, Dick VDJ, Lipalo Mokete, Yusuf KS, Tikly M, Smith A, Meiring RM. Objectively measured changes in sitting, standing and walking and their association with health outcomes of patients with knee osteoarthritis undergoing total knee arthroplasty. In preparation for submission to *BMC Musculoskeletal Disorders*.

4.3 Results (Study 2B)

Fifty-seven out of the 89 patients recruited at baseline completed the six months follow-up and 40 had sufficient ActivPAL data (FIGURE 4.4). Table 4.4 shows participants characteristics for total sample at baseline and participants who had valid and insufficient (excluded) ActivPAL activity data at six months follow up. Characteristics of participants with valid and excluded ActivPAL activity data were similar to that of the total sample recruited at baseline. However, the PROMs were significantly different in both participants with valid and excluded ActivPAL data compared to that of baseline ($p>0.05$).

Changes in LPA and SB following TKA

Table 4.5 shows comparisons of LPA and SB as well as step counts and cadence between preoperative and six months postoperatively. The percentage of walking time increased significantly from preoperative to 6 months postoperatively by 2.5% ($p=0.039$). The percentage standing time also increased by approximately 2% from the preoperative time point to six months postoperatively but the increase was not significant ($p=0.530$). The percentage of time spent sitting did not decrease significantly (4%, $p=0.079$) from preoperative to six months post-TKA.

Participants significantly increased ($p=0.0097$) their actual daily walking time from preoperative to six months after TKA by an average of 17.5 (95% CI: 4.3 – 36.0) mins/day. However, walking time at six weeks decreased compared to walking time at six months postoperatively. Likewise, participants' standing time significantly decreased ($p=0.0423$) from baseline to six weeks after TKA, but time spent standing did not increase significantly [mean (95% CI): 15.5 (95% CI: -18.9

– 21.6), p=0.3306] mins/day from baseline to six months after TKA. Overall, participants decreased their daily time spent sitting from baseline to six months after TKA, but not significantly (p=0.009) by approximately, 34.0 (95% CI: -18.9 – 106.3) mins/day. However, participants' sitting time decreased from baseline to six weeks after TKA (p=0.0365)

Participants significantly increased their daily step count from baseline to six months after TKA (p<0.001) by 1100 (522 – 1678) (mean (95% CI) steps/day. Participants' cadence (number of steps per minute) increased significantly from preoperative to six months after TKA (p=0.004) by an average of 5.0 (95% CI: 1.7-4.4) steps/min.

Association between changes in PROMs and changes in sitting, standing and walking from pre- to 6 months postoperatively

Table 4.6 shows the association between the changes in LPA and SB and the changes in PROMs from preoperative to 6 months postoperatively. The changes in participants' walking, standing and sitting times as well as their daily steps were not associated with changes in their WOMAC, KOOS, OKS and UCLA scores after controlling for gender, age, change in BMI and socioeconomic status (p>0.05).

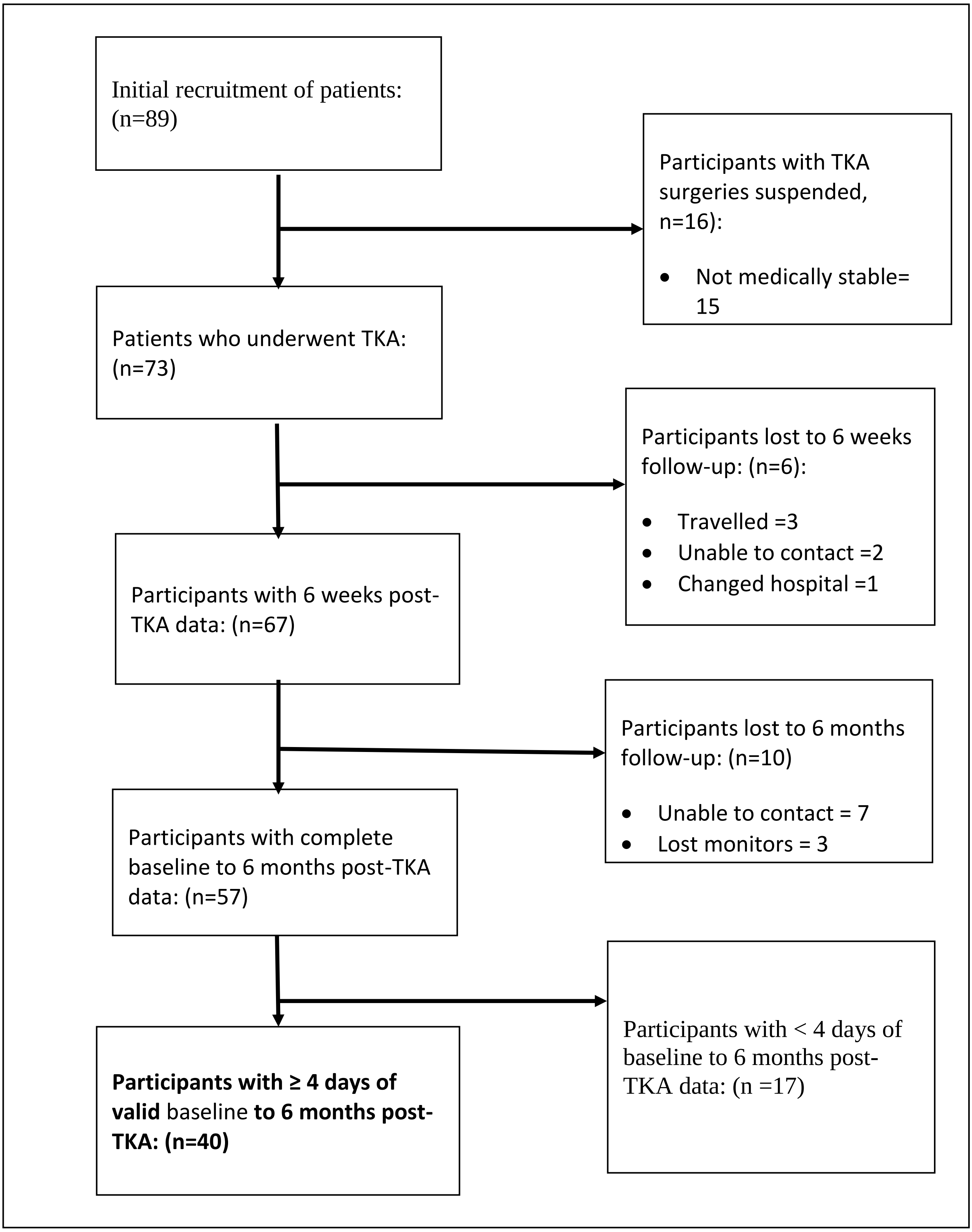

Figure 4. 4 A flow chart illustrating participants' recruitment from baseline to 6 months follow-up.

Table 4. 4 Participant characteristics

Variables	Participants with valid ActivPAL data before TKA (n=89)	Participants with valid ActivPAL data 6 months after TKA (n=40)	Participants with excluded ActivPAL data (n=17)
Age (years)	64.8 (8.7)	64.3 (9.0)	64.2 (6.3)
Gender, females, n (%)	76 (85)	35 (90)	15 (88)
Weight (kg)	84.9 (20.2)	82.9 (20.8)	83.8 (20.2)
Height (m)	1.6 (0.1)	1.6 (0.1)	1.6 (0.1)
Body Mass Index (kg/m^2)	34.9 (7.7)	33.0 (7.3)	33.9 (7.6)
LHS, median (IQR), (days)	7.0 (3.0)	7.0 (3.0)	8.0 (5.3)
Race, n (%)			
Blacks	59 (66)	25 (63)	11 (65)
Caucasians	30 (34)	15 (37)	6 (35)
Side of TKA, n (%)			
Left	31 (35)	15 (37)	7 (41)
Right	58 (65)	25 (63)	10 (59)
Socioeconomic status score	10.1 (2.8)	9.9 (3.2)	9.9 (2.7)
Educational status, n (%)			
Below High School	28 (31)	13 (33)	6 (35)
High School	49 (55)	21 (53)	10 (59)
Tertiary	12 (14)	6 (14)	1 (6)
Co-morbidity, (yes), n (%)			
Diabetes Mellitus	18 (20)	6 (15)	4 (24)
Hypertension	48 (53)	21 (53)	10 (59)
Dyslipidaemia	13 (15)	3 (8)	3 (18)
Smoking, (yes), n (%)	9 (10)	4 (10)	3 (18)
PROMs*			
WOMAC	66.3 (19.2)	5.5 (8.1)	6.3 (7.3)
KOOS	123.8 (26.0)	20.2 (17.8)	24.8 (17.7)
OKS	11.9 (10.4)	42.8 (6.3)	38.9 (6.4)
UCLA	2.3 (0.9)	5.2 (0.9)	5.0 (0.8)

LHS: length of hospital stay; SES: socioeconomic status. Age, weight, height, body mass index, SES and PROMs score are presented as mean (SD); whereas length of hospital stay is presented as median (interquartile range, IQR). The remaining data are presented as frequencies (%). *$p<0.001$

Table 4. 5 Comparison of objectively measured lower intensity activity behaviours before and after TKA

Variables	Preoperative Mean (95% CI) (n=53)	6 Weeks postoperative Mean (95% CI) (n=49)	6 Months Postoperative Mean (95% CI) (n=40)	p-value*
Valid days	5.9 (4.9 – 5.5)	5.5	6.1 (5.7 – 6.5)	0.613
Awake wear time (mins/day)	944.3 (912.3 – 976.2)	889.0 (855.7-932.8)	919.0 (891.3-946.6)	0.171
Walking, % awake wear	8.3 (7.7-10.0)	8.3 (7.4-9.3)	10.8 (9.4-12.1)	0.039*
Standing, % awake wear	32.4 (28.6-35.5)	31.2 (27.4-34.5)	34.2 (29.8-38.6)	0.530
Sitting, % awake wear	58.8 (54.4-63.2)	61.1 (57.5-64.9)	55.0 (49.9-59.9)	0.079
Walking time (mins/day)	84.2 (73.5 – 94.8)	74.9 (62.9-86.8)°	97.3 (83.5-111.1)	0.0097*
Standing time (mins/day)	307.3 (269.6-345.1)	278.1 (234.8-321.5)°°	314.9 (278.1-337.8)	0.677
Sitting time (mins/day)	554.6 (512.2-599.3)	548.6 (491.9-605.3)++	508.2 (460.0-556.0)	0.090
Steps (number/day)	2570 (2366-3189)	2122 (1994-2643)	3670 (2886-4020)	p<0.001*
Cadence (steps/min)	33 (31-34)	28 (26-32)	38 (33-39)	0.004*

All data are presented as mean (95% confidence interval- CI). * Indicates p-value between baseline and six months after TKA, adjusted for participants' age, BMI, awake wear time. °p=0.0002, decreased walking time at six weeks compared to six months after TKA; °°p<0.05 decreased standing time at 6 weeks compared to baseline (p=0.0423) and six months after TKA (0.0037); ++p<0.05, decreased sitting time at six weeks compared to baseline (p=0.0365) and six months after TKA (p=0.0002).

Table 4. 6 Univariate linear regression of changes in LPA and SB on changes in patient-reported Outcome Measures (PROMs) from preoperative to 6 months post-TKA

	Adjusted R^2	**R^2-change**	**Beta**	**B**	**95% CI**	**p-value**
Walking time						
WOMAC total	0.024	0.004	-0.070	-0.075	-0.543 – 0.693	0.798
KOOS total	0.100	0.025	-0.178	-0.169	-0.277 – 0.610	0.444
OKS	0.124	0.013	0.132	0.094	-0.261 – 0.449	0.588
UCLA	0.129	0.289	0.408	1.012	0.265 – 1.968	0.128
Standing time						
WOMAC total	0.163	0.011	0.111	26.322	-79.46– 132.10	0.612
KOOS total	0.116	0.001	-0.040	-8.44	-91.95 – 71.10	0.838
OKS	0.127	0.001	-0.032	-5.01	-71.98 – 61.97	0.880
UCLA	0.071	0.053	0.255	114.49	-65.91 – 294.89	0.205
Sitting time						
WOMAC total	0.119	0.001	-0.020	-0.019	-0.810 – 0.772	0.818
KOOS	0.199	0.008	0.104	0.085	-0.499 – 0.668	0.753
OKS	0.98	0.002	0.046	0.028	-0.553 – 0.497	0.904
UCLA	0.201	0.004	0.069	0.121	-1.111 – 1.353	0.832
Step counts						
WOMAC total	0.049	0.031	0.185	0.215	-0.385 – 0.815	0.457
KOOS	0.021	0.007	-0.094	-0.096	-0.534 - 343	0.657
OKS	0.022	0.014	-0.138	-0.107	-0.453 – 0.240	0.530
UCLA	0.221	0.145	0.600	1.320	0.542 – 2.099	0.053

Data were controlled for pre-operative age and BMI. Beta: standardized beta coefficient; *B*: unstandardized coefficient; CI: confidence interval; UCLA: University of California Los Angeles Activity Index; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Outcome Scores; KOOS: Knee Injury and Osteoarthritis Outcome Scores; OKS: Oxford Knee Score; ADL: activities of daily living; Rec: recreation. *Significant

CHAPTER 5 - DISCUSSION

Following the conclusions from the systematic review that more detailed analysis of activity behaviours especially SB, are needed following TKA, the objectives of the longitudinal study (Study 2A and B) were to objectively describe changes in the volume and pattern of PA and SB using the ActiGraph GT3X+ and to determine the association between changes in objectively measured times spent sitting, standing and walking (as measured with the ActivPAL) and changes in health outcomes (assessed with PROMs) in patients with knee OA undergoing TKA in South Africa. Overall total daily sedentary time decreased and time spent in LPA increased significantly at six months after TKA with the patients showing a reduction in SB of approximately 56 minutes and an increase in LPA of approximately 50 minutes per day. The patients also interrupted their sedentary time more frequently at six months after TKA, but the duration of these breaks was not different compared to baseline. Patients spent more time in light activity and less time in sedentary activity from morning to early evening at six months after TKA compared to baseline. In addition, patients significantly increased their daily number of steps and total daily time spent walking from baseline to six months postoperatively and they showed a decrease of approximately 34 minutes per day in their time spent sitting (but this was not statistically significant), however, changes in these low intensity activities were not associated with changes (or improvements) in the patients' self-reported outcome measures.

An important finding of the current study is the significant reduction in total time spent sedentary from baseline (10.8 hours/day, 70.1% of awake wear time) to six months after TKA (9.9 hours/day, 64.0%). This percentage reduction in time spent sedentary translated into a decrease of almost one hour of sedentary time per day at six months after TKA. Although in the current study, the amount of time spent in SB at six months after TKA was higher than that of the knee OA patients of Brandes et al. (53) study (7.0 hours/day, 56.5% of awake wear time), and lower than that of both hip and knee OA patients of Harding et al. (40) study (11.6 hours/day, 83% of awake wear time), the decrease in sedentary time of this magnitude has not yet been reported in TKA patients following their surgery.

Along with the observed decrease in sedentary time for the patients in this study, increases in volume and patterns of LPA at six months after TKA were found. This translated to an 18.3% improvement in LPA at six months after TKA. With no significant difference being observed in the time participants spent in MVPA, it is likely that the SB was offset with LPA. In addition to the changes in volumes of activity behaviours (particularly at the lower intensities, that is, SB and LPA), there were differences in the patterns of how activity behaviours were accumulated. Time spent in prolonged SB of at least 30 minutes significantly decreased at six months after TKA. Furthermore, the time spent sedentary was interrupted more frequently after TKA with LPA. This study of South African knee OA patients presents a reliable data owing to a good methodological approach. In the current study, activity was monitored with a tri-axial ActiGraph GT3X accelerometer for seven consecutive days using a 24-hour protocol and only included patients with at least four valid days of accelerometry recordings (61). Previous studies have either monitored activity of participants in less than three days (39,42,53,62) or between four and seven days (40,64).

One of the novel findings of this study is the detailed presentation of the hourly variations in time spent in lower intensity activities (SB and LPA). Understanding the hourly patterns of SB and LPA provides a useful source of information for physician monitoring of patients and for informing targeted interventions with the ultimate aim of improving overall health and quality of life patients with knee OA undergoing TKA. Patients of this study accumulated similar volumes of SB and LPA in the early hours of the day (6h00-10h00) before TKA. However, following TKA, there was a noticeable shift in total amounts of sedentary and light activity accumulated over the course of the day, but particularly at certain times of the day. Compared to baseline, there was less time spent in SB and more in LPA between 11h00-19h00 at six months after TKA. Light PA is associated with purposeful movements accumulated during performances of activities of daily living (ADL) [11]. The increase in LPA and decrease in SB at a time of day when the patients were likely to be engaged in household, social and occupational activities has implications for quality of life of the patients and may offer an explanation as to why such great improvements in activity behaviours were observed following TKA. It has been shown that decreasing time spent sedentary and increasing LPA may be important for maintaining cardiometabolic health in adults independent of MVPA [63,64].

Consistent in all of the studies that have assessed PA in patients before and/or after TKA, is the observation of a low accumulation of MVPA. In this study, less than 1.0% of the daily awake wear time was spent in MVPA at six months after TKA. Despite the high rate of success associated with TKA, a lower recovery rate compared to total hip arthroplasty (THA), post-surgical pain and quadriceps muscle weakness have all been found to mitigate physical functioning (330,29,331,332). In the current study, less than a third of the patients met the PA guidelines at baseline and six months after TKA. All of the patients in the current study had advanced knee OA prior to surgery and they may have had underlying musculoskeletal damage as a consequence of the knee OA, thereby inhibited more intense movements. Patients were also on average 65 years of age and most older adults do not achieve the recommended PA guidelines even in the absence of a musculoskeletal disorder (333). However, the patients' number of steps per day both at baseline and six months post-surgery is consistent with the reported values for healthy 65-69 year adults in the National Health and Nutrition Examination Survey (NHANES) (3302-5269 steps/day) (334). The patients in this sample may therefore have already been relatively lightly active and may have been further motivated to increase their activity post-surgery in the lower intensity activities. A longer duration of recovery may allow such patients to adopt a more moderately intensively active lifestyle (39).

As expected, scores of WOMAC, KOOS, OKS and UCLA as well as active knee ROM improved from baseline to six months after TKA. These results are in agreement with several prior studies (39,40,42,57,58). Although, PROMs are subjective, and have some limitations (49), they provide as useful information as the objectively measured PA and SB and have implications for both clinical practice and research purposes. These improvements in patient-reported activity and physical functioning may be due to considerable improvements in pain and stiffness or increased ROM at the operated knee with improved ability to perform ADLs.

As already highlighted, patients significantly improved their low intensity activity behaviours (SB and LPA) measured objectively through accelerometry (with ActiGraph GT3X+) and also had improvements in their health outcomes (i.e. the PROMs) at six months after TKA. Hence, there was a need to use activity monitors shown to be valid in measuring low intensity activities that are incidental in daily routines (i.e. times spent sitting, standing and walking) and to determine their associations with changes or improvements in the PROMs. The times spent sitting, standing and walking as well as daily step counts were measured objectively using the ActivPAL activity monitor, which accurately measures low intensity activities in older adults (198,232,234,335). The results showed that patients reduced their percentage of time spent sitting which on average, amounted to a daily decrease of over half an hour. The time spent sitting at six months after TKA was lower than those of other two previous studies (64,68) that have reported their participants spent 10.3 (64) and 10.4 (68) hours/day sitting at 12 months after TKA. The time spent sitting by patients of this study is similar to typical levels of the general population (267). The observed reductions in sitting time may have been as a result of interruptions in sitting with the observed increases in walking and standing, given that LPA and SB are inversely related (336).

Patients spent more of their waking wear time standing than walking at six months after TKA, however, the time spent standing was over twice that reported in a previous study (42) at six months after TKA. Only one other study, has reported a significant increase in the time their participants spent walking (5.8% to 6.7% of awake wear time), however activity was assessed at one year after TKA (68). The percentage increase in participants' walking time in this study showed that on average, they walked nearly half an hour longer per day at six months postoperatively compared to before surgery. Although the intensity of activity is probably not MVPA (as demonstrated by prior studies (40,59,64)) and also from the ActiGraph data in this study, the data still show that patients moved more and improvements in any movement behaviours (even those of light intensity) may prove to be beneficial in this type of patient (72). Indeed, the newly released 2018 PA guidelines recommend that for individuals unable to meet the PA guidelines replacing sedentary time with LPA is beneficial (264).

In line with an increase in walking time, patients accumulated a greater number of steps per day at six months postoperatively compared to before TKA. Walker et al. (62) in their study, reported on average an increase of 4900 steps per day at 6 months after TKA.

Furthermore, similar to the findings of this study, Brandes et al. (53) found an increase of 1006 steps per day at six months after TKA. However, in the aforementioned studies, physical activity was measured for only one day, which is shorter than the recommended three to seven days for monitoring activity in adult (61), hence data may not likely to be representative of activity behaviour of a typical day. The step counts of the participants at six months after TKA are within the 3500-5500 steps per day recommended for older adults living with disabilities and chronic illnesses (337). In addition to an increase in total daily steps, cadence also improved at six months after TKA. This finding is in agreement with those of a previous study at one year after TKA (59). Participants walked relatively faster than before TKA, however, the steps rate was lower than the 100 steps per minute threshold of moderate intensity (338) suggestive of a walking intensity of low/light activity. Although, following TKA, average daily cadence is expected to improve (318), walking at a slower pace compared to the moderate intensity threshold in patients with TKA is to be expected in older adults with mobility impairments. This type of intensity target may be more feasible for patients following TKA and therefore the findings of this study may inform postoperative interventions for motivating and increasing ambulatory functions of patients within the light activity intensity category.

The changes in activity behaviours were expected to translate to an improvement in physical functioning and although PROMs improved post-operatively, the observed changes in participants' times spent sitting, standing and walking as well as step counts were not associated with the participants' improvements in health outcomes. Previous studies have reported that participants' self-reported activity, physical function and quality of life improved after TKA but not the objectively measured overall PA or PA of high intensity (54,55,284). Adding to this, this study shows that an increase in LPA and a decrease in SB incidental in ADLs are not related to improvement in participants' self-reported activity, physical function and quality of life. The lack of association between improvements in low intensity activity behaviours (that is, an increase in LPA and a decrease in SB) and PROMs could be due to the inherent limitations of self-report measures. The PROMs as self-report measures may have poor validity and reliability and bias regarding recall (48,49). Additionally, it has been observed that levels of patients' pain and exertion during performance of functional tasks greatly influence their PROMs scores (339), which may lead to underestimation or overestimation of functional status. Therefore, exaggerating behaviours may be eliminated when one measures activity objectively which is a strength of this study. Self-perceived improvement in health status is subjective thus there may be other factors that dictate whether someone actually improves or reports an improvement. The drivers of PA change following TKA (or any musculoskeletal recommended surgery) should be investigated in future studies. This is an important concept that should be explored in future studies of both healthy and diseased populations.

Generally, with the exception of improvements in the PROMs, objectively measured activity behaviours (by both the ActiGraph GT3X+ and ActivPAL) did not improve at six weeks after TKA. Physical activity decreased while SB (including time spent sitting) increased six weeks following TKA. However, LPA improved and SB decreased at six months after TKA. It has been explained that patients are discharged home with limited functions compared to the level before TKA (30) and that sequels of operation such as pain and complications mitigate activities in the subacute phase of recovery (340). The findings at six weeks after TKA were expected as soft tissue healing may not be optimal six weeks after the surgery (341). Therefore, postoperative follow-ups that are longer than six week would be more realistic in observing changes in objectively measured activity behaviours.

The current study is the first to explore activity behaviours at all intensities in a population living in a low to middle income country (South Africa) and this may be one of the reasons for the difference between the findings of this study and others that have reported no or marginal improvements in activity behaviours following TKA (39,40,42,57–59). This study was conducted in patients of low socioeconomic status (with particularly, low educational background) compared to other studies done in high-income countries. Changes in daily routine and nature of work at home and workplace (due to urbanization and automatism of work and life) may result in higher daily participation in SB (281,282). Whereas individuals from high-income countries may be able to increase leisure-time PA in the case of activity reduction due to work schedules (342), their counterparts in lower-income groups (due to poor economic climates) tend to improve PA by performing activities of daily routines related to work, domestic chores and transport (343). Furthermore, the motivation to changes in activity behaviours in patients with musculoskeletal disorders may vary from one socioeconomic group to the other. Therefore, the inherent motivation to independently perform ADLs and return to work post-operatively may have resulted in improved activity behaviours of patients involved in this study. Herbolsheimer et al (74) indeed showed that the impact of knee OA on activity behaviour patterns of its sufferers varies from one socioeconomic group to the other (74).

The findings of this study have implications for postoperative interventions for further improving activity behaviours. This study supports the notion that targeted interventions may focus on increasing LPA and decreasing SB, especially at 6 months postoperatively, where functional recovery appears to be optimal (29,54,140). Long term postoperative interventions aimed at offsetting sedentary time with LPA or task-oriented activities performed during ADLs may sustain recovery of functions, quality of life and physical activity in the long term. Such interventions should be clinic-based and supervised exercises (including land or water-based exercises), which are found to be safer with long-term beneficial effects than home-based and/or remotely supervised exercise programmes (344). Furthermore, postoperative interventions comprising strengthening, endurance, balance and flexibility training may maintain and improve physical function and overall physical activity (345–347). Additionally, interventions that can motivate and support TKA patients to adopt an active lifestyle are needed. For example, using mobile messages to prompt interruptions in sedentary time (348).

Study limitations and strengths

There are a few limitations associated with this study. There was a high attrition rate during follow up which decreased the total number of participants completing the six-month follow up. Additionally, some data were excluded from the analysis due to invalid number of hours for a complete day criterion. This may be as a result of patients' failure to put on the ActiGraph GT3X+ having removed it before showering/bathing or swimming and the ActivPAL falling off during the week-long activity monitoring when the water-proof tapes lost their adhesiveness. However, the characteristics of the excluded patients were similar to those included in the analyses. The use of accelerometers comes with the challenge of different algorithms and decision rules for cut points for PA and SB. This makes comparison with other studies limiting in addition to the fact that there is a dearth of studies that have used both ActiGraph GT3X+ and ActivPAL in measuring activity in patients undergoing TKA. Thus, it is important to have accelerometer cut point algorithms validated for specific populations (for example, in those with musculoskeletal disorders) (217). However, there are newer processing techniques that make use of the raw accelerometry data (349,350). Most importantly, waist-worn accelerometers (including ActiGraph GT3X+) do not always adequately measure activities involving upper body or upright activity behaviours of low ambulatory components such as cycling (351).

The use of pain medications postoperatively may have resulted in erroneous self-report improvement in pain and less difficulty in physical functioning. This may have influenced the observation of no association between low intensity activities and PROMs. However, biological, psychological and social factors are important in properly explaining pain in knee OA patients (110). Furthermore, the lack of translated versions of the knee-specific functional questionnaires may have also limited a great deal of responses from patients due to language barrier as English is not the first language for majority of patients who took part in this study. For example, WOMAC, KOOS and OKS require patients to rate their level of pain and/or difficulty in performing ADLs on a five point Likert scale (never, mild, moderate, severe and extreme); but such rating may be very confusing (for example, the distinction between mild and moderate) for those who are not fluent in the English language. This is why using objective methods such as accelerometry (as used in this study) to measure activity behaviours is worthwhile in eliminating any language barriers associated with the use of questionnaires. There is however, a need to validate the knee OA-specific functional questionnaires in the South African OA population and/or modify them if necessary.

This study supports using objective methods for assessing improvements in functional ability of patients after TKA. Following TKA, improvement in ADL can be objectively assessed since improvement in low intensity activities (LPA and SB) without a change in MVPA suggest improved functional ability and quality of life (215). This study utilised two accelerometers or activity monitors (ActiGraph GT3X+ and ActivPAL) to generate comprehensive data to describe activity behaviours (at all intensities) of patients with knee OA undergoing TKA. Assessing SB by postures using the ActivPAL gives a more valid and reliable estimates of times spent sedentary or sitting in patients with knee OA undergoing TKA. Another strength of this study is that it is the first to report data on the patterns of activity behaviours (SB and PA) of patients from a low-middle income country (South Africa). Again, the current study has examined the association between objectively measured activities of lower intensities and self-reported functional outcomes. Most importantly, this study demonstrates focusing on assessing low intensity activities of patients with knee OA as these activities are more likely to change following TKA. Furthermore, the findings of this study highlights the need for several future studies especially, studies on interventions that may improve LPA and decrease SB following TKA.

Taken together, the systematic review (Study 1) revealed that the majority of the studies reported no changes in SB (from the few studies that have been conducted in high-income countries) following TKA and that the patterns of accumulation of SB have not been studied before and after TKA. However, with knee OA patients from a low-middle income (South Africa), the longitudinal study (Study 2A and B) has demonstrated an increase in LPA and a decrease in SB and an improvement in patient-reported pain, stiffness and physical function at six months after TKA. In particular, with respect to the objective measures, the biggest changes were with respect to SB where there was a decrease in overall time spent in SB and an increase in the number of breaks in SB, which appeared to be replaced by LPA. However, patients did not achieve the current PA guidelines because no improvement to MVPA occurred. Patients' volume and average daily cadence increased significantly, while their sitting time tended to decrease at six months after TKA. However, there were no associations between changes in objectively measured low intensity activities and changes in patient-reported outcome measures at six months after TKA. The fact that patients came from a low-middle income country suggests that there may be different needs in different populations that drive change in activity behaviours in patients with musculoskeletal disorders. This comprehensive analysis of detailed daily activity behaviours can be used to employ feasible interventions for increasing the duration of LPA bouts (standing and walking) and decreasing prolonged sedentary bouts (sitting) to improve quality of life and overall health following TKA. Furthermore, both objective and subjective measures should be used to properly assess improvements in health outcomes following TKA.

CHAPTER 6 - CONCLUSIONS

In this thesis I set out to determine whether objectively measured PA and SB (measured using two accelerometers) changed in patients after having undergone TKA. The novelty of this research was that these studies had not yet been done in a low to middle income country before. Furthermore the use of two accelerometers and the detail of activity behaviours obtained from these devices had not been previously presented. In addition, there have been no systematic reviews on the assessment of SB in these populations, which is important because SB is a part of the activity spectrum and has its own implications for health and physical functioning. Based on previous literature that PA does not seem to change following TKA and knowing that SB is an important part of activity behaviour research, I first conducted a systematic review to determine what the current view was on the effects of TKA on SB. The findings of the systematic review showed that SB does not change following TKA, however, there was insufficient evidence as few studies have assessed SB before and after TKA. This finding as well as the findings of previous systematic reviews on PA changes after TKA justified the need to include investigating activity behaviours at all intensities (SB, LPA and MVPA) in these patients.

The next objectives of this thesis were therefore, to describe changes in the objectively measured patterns of accumulation of habitual PA and SB of patients with knee OA undergoing unilateral primary TKA and to also determine changes in the traditionally used PROMs. The use of accelerometry allows for the discernment of activity thresholds between SB, LPA and MVPA. The ActiGraph data gave information not only on total volume of activity but also how that activity was accumulated throughout the day (bouts of activity) and the variation in activity across the whole day i.e. from morning to evening. I was able to look at how those patterns changed in patients following TKA and this study revealed some surprising results. I found that daily total volume and patterns of SB and LPA significantly improved six months after TKA. Most importantly, it was found that patients spent more time in light activities (e.g. walking) and less time in sedentary activities (such as sitting) throughout the waking day at six months after TKA. However, similar to findings of previous studies, patients could not improve their MVPA and as a result, very few of the patients met the current PA guidelines. These findings support the fact that, current PA guidelines may be unrealistic and too high a criterion for older adults with end-stage knee OA undergoing TKA to comply with or adhere to. This thesis therefore, supports the need for specific PA guidelines for patients with musculoskeletal deficits such as knee OA. Furthermore, there is a need for a paradigm shift in public health messages and clinical guidelines for promoting low intensity activities rather than MVPA in patients with musculoskeletal disorders.

Because there was a change in activities at the lower end of the movement spectrum, I further investigated improvements in the low intensity activities that are incidental in daily routines, which are perhaps, the most important activities for older adults undergoing TKA. I also wished to determine whether these changes were associated with the changes in PROMs. Using the ActivPAL that measures activity behaviours relevant to lower functioning activities, I found that patients' daily time spent walking significantly improved with a reduction in their time spent sitting per day (although not significant) at six months after TKA. The results further support the need to focus on improving low intensity activities that occur in performance of ADLs. However, there was no association between improvement in health outcomes and changes in low intensity activities six months postoperatively. It is likely that patients may have not accurately reported their improvements in pain, physical functioning and quality of life and consequently, improvements in perceived functional ability are not related to objectively measured activity. These results mean that solely relying on PROMs as a measure of improvements in patients' treatment outcome may be spurious; therefore it is important to include objective measurements for accurate assessment of patients' outcomes before and after TKA.

The findings of both the systematic review and the longitudinal study (Study 2A and B) show that more studies assessing activity behaviours of knee OA patients before and after TKA are need to adequately evaluate the effects of the surgery on PA and SB. Assessing the patterns of PA and SB are feasible especially when using objective methods (such as accelerometry) that are able to accurately and reliably quantify low intensity activities relevant to older adults undergoing TKA.

Overall, this thesis extends the body of knowledge on activity behaviours of patients with knee OA undergoing TKA, especially from low to middle income countries. This thesis demonstrates that assessing changes in activity behaviour patterns is important following TKA as it may reveal subtleties in change that would increase our understanding about which activities to target at improving them in the knee OA population. Therefore, this thesis seems to draw the attention to a need for a paradigm shift from focussing on MVPA alone or total activity, as has been the case in most previous studies, to low intensity activity behaviours following TKA. In addition, the thesis shows that it is more feasible to replace or interrupt sedentary time (e.g. sitting) with LPA (such as standing and/or walking) than with MVPA. It is increasingly becoming clear about the impact of the low intensity activities on health and the role a good balance of their accumulations play in health and disease. Interestingly, the latest 2018 PA guidelines recommend increasing LPA to replace SB in people who are unable to do more MVPA or meet the PA guidelines. To the best of my knowledge, this thesis is the only study that has been conducted in a low-middle income country like South Africa but has generated findings that are contrary to those from high-income or developed countries. Whereas studies from high-income countries reported very little or no change in PA and SB following TKA, this study of South African knee patients showed improvements in PA (particularly LPA) and SB. It appears that changes in PA and SB of knee OA patients differ after TKA between low-middle income and high-income countries. However, more studies are needed to elucidate this trend.

Historically, the PROMs have been used clinically to assess improvements in functional ability and success of TKA for knee OA. Since improvements in the low intensity activities in ADL (as measured by the ActivPAL) were not related to improvements in

PROMs for pain and self-perceived physical function, may mean that both instruments do not measure the same construct. In addition, it may also mean that improvement in pain and self-perceived physical functioning may not necessarily result in improved PA or decreased SB. Furthermore, PROMs have low validity and reliability and they come with a language barrier especially for populations in which the PROMs have not been validated for use. Therefore, using accelerometry to measure PA and SB as a surrogate measure of functional ability may be a promising way of objectively evaluating patients' health outcome and surgical success after TKA.

A summary of the hypothesis tested and the findings is found in Table 6.1.

Table 6. 1 Hypothesis tested in this thesis.

Name of study	Study objectives	Hypothesis	Main finding
Study 2A	To determine the changes in volume and pattern of objectively measured physical activity and sedentary behaviour following total knee arthroplasty.	Objectively measured volume and pattern of PA and SB would not improve at six months after TKA.	Objectively measured total daily volume and patterns of accumulation of LPA and SB improved significantly at six months following TKA.
Study 2B	To determine objectively measured changes in sitting, standing and walking and their association with health outcomes of patients with knee osteoarthritis undergoing total knee arthroplasty	Patient-reported outcome measures for pain, physical function and quality of life would improve six months following TKA. There would be associations between changes in the PROMs and changes in objectively measured times spent sitting, standing and walking.	The PROMs for pain, physical function and quality of life improved six months following TKA but improvements in the PROMs were not associated with the objectively measured changes in times spent sitting, standing and walking.

PROMs: patient-reported outcome measures; TKA: total knee arthroplasty; LPA: light physical activity.

Future research

The findings of this thesis warrant further studies on changes in PA and SB following TKA. Future clinical trials of longitudinal designs with longer follow-up objectively measuring PA and SB before and after primary TKA are needed to better understand the trajectories of activity change following TKA. This is because at post-surgery, the rehabilitation process can be slow and different for different people. The findings of this thesis also direct more studies from low-middle income countries especially from other African countries to better understand what changes PA and SB of people from developing countries with and without knee OA. Of equal importance, is the need for informed targeted interventions for improving LPA and decreasing SB of knee OA patients undergoing TKA. Additionally, future studies should further test the association between PROMs and all levels of PA intensities following TKA, as this may buttress the need for increased use of objective instruments (such as accelerometers) for measuring PA and SB as well as functional ability. The findings of this thesis also warrant future investigations into whether if quality of life, sleep and depression and other aspects of daily life improve following TKA. This may be very important as this thesis has confirmed a way of objectively assessing functional ability and the next step may be investigating if other behaviours also improve. Furthermore, validation of knee-specific questionnaires in knee OA population that would enable the development of a simple clinical tool for use in knee OA population in South Africa is worth investigating. Finally, future systematic reviews should employ a more quantitative approach for synthesizing findings of evidence for concluding the effects of TKA on SB.

In conclusion, primary total knee arthroplasty was effective in improving objectively measured volume and patterns of low intensity activity behaviours (i.e. light intensity physical activity and sedentary behaviour) at six months after TKA. Total knee arthroplasty also improved patient-reported health outcomes, however, improvements in the health outcomes were not associated with improvements in the low intensity activities. This thesis supports the need for targeted interventions for improving light physical activity and decreasing sedentary behaviour for improved quality of life and overall health. Furthermore, both objective and subjective measures should be used to accurately and reliably assess patients’ health outcomes following TKA.

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APPENDICES

APPENDIX A – Information sheet

School of Physiology

Faculty of Health Sciences, University of the Witwatersrand, Johannesburg
7 York Road, Parkton, 2193 · Tel: +27-11-717-2363 · Fax: +27-11-643-2765

INFORMATION SHEET

Assessment of physical activity in patients with knee osteoarthritis

Good day.

My name is Emmanuel, and I along with my co-investigators from Wits University would like to invite you to take part in our study. We are interested in looking at whether physical activity and sitting time change after total knee replacement surgery.

If you would like to take part in our study, we would like to meet with you at the hospital twice before you have your surgery and twice after you have had your surgery. These meetings will be on the same days that you come in to see the doctor who is treating you. When you come in to see the doctor, we would like you to fill out some questionnaires. The doctor or the researcher will help you fill out these questionnaires. At each of these visits we will also give you two small devices to war that will measure your activity. The approximate times that we would like you to do these things for us are at some of the visits before and after your knee surgery: 1) two weeks before the surgery once you have been taken off any anti-inflammatory medications, 2) six weeks postoperatively and 3) six months postoperatively.

School of Physiology

Information that is obtained from you and the ActivGraph and ActivPAL will be kept strictly confidential. We would like to emphasize that participation is completely voluntary and if you do not want to continue with the study, you can withdraw at any time without prejudice. The data will be made available to you should you be interested in the outcome of the study.

Thank you for considering participation in this study. Please read the information sheet carefully before signing the consent form*. If you have any queries, please contact myself Emmanuel. Tel: 0832065111, Email: 1345783@students.wits.ac.za or Rebecca, Tel: 0117172161, Email: Rebecca.Meiring@wits.ac.za.

If you have any doubts to your rights as a participant please feel free to contact Ms Zanele Ndlovu or Mr Langutani Masingi, Medical School, Parktown, Philip Tobias Building, 2nd Floor, Cnr York Road and Princes of Wales Taerrace, Mon-Fri 08h00-17h00, Tel:011-717-1234/1252/2700 or Langutani.Masingi@wits.ac.za. Chair of the Human Research Ethics Committee: Prof Cleaton-Jones, peter.cleaton-jones1@wits.ac.za, 0117172301.

APPENDIX B – Informed Consent

School of Physiology

Faculty of Health Sciences, University of the Witwatersrand, Johannesburg
7 York Road, Parkton, 2193 · Tel: +27-11-717-2363 · Fax: +27-11-643-2765

CONSENT TO ACT AS PARTICIPANT IN RESEARCH

I____ (full name and surname)

agree to participant in the study titled: The Effect of unilateral knee arthroplasty on objectively measured physical activity and sedentary behaviour outcomes.

The procedures/questionnaires have been explained to me and I understand and appreciate their purpose, any risks involved, and the extent of my involvement. I have read and understand the attached information sheet.

I understand that the procedures form part of a research project and may not provide any direct benefit to me.

I understand that all experimental procedures have been sanctioned by the Committee for Research of Human Subjects, University of the Witwatersrand, Johannesburg, South Africa.

I understand that my participation is voluntary and that I am free to withdraw my participation from the project at any time without prejudice.

____________________________ ______________________
Participant's name and signature Date

____________________________ ______________________
Investigator's name and signature Date

APPENDIX C – General health and socioeconomic questionnaire

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

APPENDIX D – Pain and sleep questionnaire

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.

No pain at all ____ Worst pain I have ever felt

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.

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 . . .**

1. when walking on a flat surface?

none	mild	moderate	severe	extreme
❑	❑	❑	❑	❑

2. when going up or down stairs?

none	mild	moderate	severe	extreme
❑	❑	❑	❑	❑

3. at night while in bed? (that is - pain that disturbs your sleep)

none	mild	moderate	severe	extreme
❑	❑	❑	❑	❑

4. while sitting or lying down?

none	mild	moderate	severe	extreme
❑	❑	❑	❑	❑

5. while standing?

none	mild	moderate	severe	extreme
❑	❑	❑	❑	❑

Study Coordinator Use Only

PAIN1 ____

PAIN2 ____

PAIN3 ____

PAIN4 ____

PAIN5 ____

WOMAC Osteoarthritis Index LK3.1 (IK)

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 ____

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 . . .**

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

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 ____

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 ____

APPENDIX F – KOOS questionnaire

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

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

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 questionnair

APPENDIX G – OKS questionnaire

Oxford Knee Score (OKS)

English version for the United Kingdom

Prior to completing the Questionnaire please complete the following:-

Today's Date:

|_|_| |_|_| |2|0|_|_|
D D M M Y Y Y Y

On which side of your body is the affected joint, **for which you are receiving treatment.**

Left ❑
Right ❑
Both ❑

If you said 'both', please complete the first questionnaire thinking about the right side. A second questionnaire, for the left side, will follow.

PROBLEMS WITH YOUR KNEE

Tick (✓) one box for every question.

1. During the past 4 weeks...

How would you describe the pain you usually have from your knee?

None	Very mild	Mild	Moderate	Severe
☐	☐	☐	☐	☐

2. During the past 4 weeks...

Have you had any trouble with washing and drying yourself (all over) because of your knee?

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
☐	☐	☐	☐	☐

3. During the past 4 weeks...

Have you had any trouble getting in and out of a car or using public transport because of your knee? (whichever you would tend to use)

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
☐	☐	☐	☐	☐

4. During the past 4 weeks...

For how long have you been able to walk before pain from your knee becomes **severe**? (with or without a stick)

No pain/More than 30 minutes	16 to 30 minutes	5 to 15 minutes	Around the house only	Not at all/pain severe when walking
☐	☐	☐	☐	☐

5. During the past 4 weeks...

After a meal (sat at a table), how painful has it been for you to stand up from a chair because of your knee?

Not at all painful	Slightly painful	Moderately painful	Very painful	Unbearable
☐	☐	☐	☐	☐

6. During the past 4 weeks...

Have you been limping when walking, because of your knee?

Rarely/never	Sometimes, or just at first	Often, not just at first	Most of the time	All of the time
☐	☐	☐	☐	☐

7. During the past 4 weeks...

Could you kneel down and get up again afterwards?

Yes, easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, impossible
☐	☐	☐	☐	☐

8. During the past 4 weeks...

Have you been troubled by pain from your knee in bed at night?

No nights	Only 1 or 2 nights	Some nights	Most nights	Every night
☐	☐	☐	☐	☐

9. During the past 4 weeks...

How much has pain from your knee interfered with your usual work (including housework)?

Not at all	A little bit	Moderately	Greatly	Totally
☐	☐	☐	☐	☐

10. During the past 4 weeks...

Have you felt that your knee might suddenly 'give way' or let you down?

Rarely/ never	Sometimes, or just at first	Often, not just at first	Most of the time	All of the time
☐	☐	☐	☐	☐

11. During the past 4 weeks...

Could you do the household shopping on your own?

Yes, easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, impossible
☐	☐	☐	☐	☐

12. During the past 4 weeks...

Could you walk down one flight of stairs?

Yes, easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, impossible
☐	☐	☐	☐	☐

Finally, please check back that you have answered each question.

Thank you very much.

APPENDIX H – UCLA activity questionnaire

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

APPENDIX I - Ethics clearance certificate

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

APPENDIX J – Peer-reviewed journal article 1

Meiring et al. BMC Musculoskeletal Disorders (2016) 17:281
DOI 10.1186/s12891-016-1141-5

BMC Musculoskeletal Disorders

STUDY PROTOCOL

Open Access

Rationale, design and protocol of a longitudinal study assessing the effect of total knee arthroplasty on habitual physical activity and sedentary behavior in adults with osteoarthritis

Rebecca M. Meiring[1*], Emmanuel Frimpong[1], Lipalo Mokete[2], Jurek Pietrzak[2], Dick Van Der Jagt[2], Mohammed Tikly[3] and Joanne A. McVeigh[1,4]

Abstract

Background: Physical activity levels are decreased and sedentary behaviour levels are increased in patients with knee osteoarthritis (OA). However, previous studies have shown that following total knee arthroplasty (TKA), objectively measured physical activity levels do not change compared to before the surgery. Very few studies have objectively assessed sedentary behaviour following TKA. This study aims to assess patterns of objective habitual physical activity and sedentary behaviour in patients with knee OA and to determine whether these change following TKA.

Methods: Patients diagnosed with knee osteoarthritis and scheduled for unilateral primary total knee arthroplasty will be recruited from the Orthopaedic Division at the Charlotte Maxeke Johannesburg Academic Hospital. Eligible participants will have assessments completed one week before the scheduled arthroplasty, six weeks, and six months post-operatively. The primary outcomes are habitual physical activity and sedentary behaviour which will be measured using accelerometry (Actigraph GTX3+ and activPal monitors) at the specific time points. The secondary outcomes will be improvements in osteoarthritis-specific quality of life measures using the following questionnaires: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Knee injury and Osteoarthritis Outcome Score (KOOS), Oxford Knee Score (OKS), Knee Society Clinical Rating System (KSS), UCLA activity index; subjective pain scores, and self reported sleep quality.

Discussion: The present study will contribute to the field of musculoskeletal health by providing a rich detailed description of the patterns of accumulation of physical activity and sedentary behaviour in patients with knee OA. These data will contribute to existing knowledge using an objective measurement for the assessment of functional ability after total knee arthroplasty. Although studies have used accelerometry to measure physical activity in knee OA patients, the data provided thus far have not delved into the detailed patterns of how and when physical activity is accumulated before and after TKA. Accurate assessment of physical activity is important for physical activity interventions that target special populations.

Trial registration: NCT02675062 (4 February 2016).

Keywords: Accelerometery, Osteoarthritis, Sedentary behaviour, Physical activity, Knee arthroplasty

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Background

Osteoarthritis (OA), the most common joint disorder, causing disability and loss of function, affects over 40 % of adults (aged 70 years and older) worldwide [1]. Concomitant with disrupted sleep, depression, increased sedentary behaviour, less physical activity, obesity, and polypharmacy, OA is associated with a decreased quality of life. Most occurrences of OA (41 %) are in the knee [2]. Although data are lacking from low to middle income countries, the few studies that have been done have shown that similar to populations from the US, knee OA is more common than is hip OA in African populations [3–5].

Pain is often a major contributing factor that impedes physical activity and reduces functionality in patients with knee OA [6, 7]. Approximately 80 % of individuals with OA experience limitations in movement and 25 % of individuals with OA experience limitations in major activities in their daily lives [7, 8] and the more severe the pain, the greater the degree of physical disability [9]. Conversely higher physical activity is associated with a lower risk of OA related joint pain and stiffness [10].

People with knee OA are physically inactive and highly sedentary

Studies that have used objective measures to evaluate physical activity and sedentariness in patients with knee OA have found that 41.1 % of males and 56.5 % of f-emales with knee OA are inactive [11], that is they do not meet the recommended physical activity guidelines [11–15]. In addition to the total amount of time spent in physical activity (PA) being important for health outcomes in adults [16, 17], there is an emerging body of evidence to show that the patterns of how physical activity and sedentary time are accumulated may also have implications for health. There remains a paucity of literature describing the detailed patterns of how physical activity is accumulated in patients with knee OA.

Sedentary behaviours (SBs) are those with an energy expenditure of less than 1.5 metabolic equivalents (METS) [18, 19]. In older men, interruptions to sedentary time is associated with better muscle quality in older men [20]. Adults with OA who are more sedentary experience a greater loss in functional capacity compared to adults who are less sedentary [12, 21–23], and this relationship appears to be independent of time spent in moderate to vigorous physical activity [21]. The number of daily hours patients with OA spend being sedentary (9.8 h) [12, 24] is similar to that reported in healthy adults (9.2 h) taking part in the European RISC study [25]. Additionally sedentary time in patients with knee OA is often elevated prior to knee replacement surgery [12, 26]. However detailed data describing how and when sedentary behaviour is accumulated are lacking in this population.

Physical activity and total knee arthroplasty

Compared to the other rheumatic diseases, pharmacological treatment for OA is relatively unsatisfactory [27]. Although non-surgical treatment is the primary choice of treatment in OA patients [28], the main indication for total knee arthroplasty (TKA) is failure of conservative treatment; essentially pain that is not responsive to both pharmacological and non-pharmacological measures together with an increasing difficulty with activities of daily life in the context of advanced degenerative changes of the knee. There are no accurate figures for the number of knee replacements done in South Africa as there are no established registries. The main aim of the surgery is to alleviate pain and restore quality of life. Generally, patients are being operated on earlier in the progressions of the disease as it is recognized that quality of life is more likely to be restored in those patients, as opposed to patients with advanced disease where quality of life can be improved but not necessarily restored. As such regaining of functional ability allowing for restoration of habitual activity levels as near to normal as possible and a reduction in sedentary time are important goals for post-operative knee OA patients. Hence a desirable outcome that could be considered useful in assessing the regaining of functional ability would be to determine the number of patients who meet current physical activity guidelines [29] (including a reduction in sedentary behaviour) following TKA.

Physical activity and functional ability outcomes have historically been measured using self-report, but a more objective and quantified understanding of the impacts of knee arthroplasty on physical and functional ability are needed. Studies using interview based questionnaires have shown improved mobility benefits of TKA in developed countries [30], although data in low to middle income countries are scarce.

Assessment of functional ability in knee OA patients following TKA

Studies using self-report have shown positive improvements in functional ability (ability to perform activities of daily living), pain and quality of life after TKA [31–33] while others have reported no significant improvements on health outcome measures following TKA [31, 34–36]. Self-report may also be open to bias and inaccuracy [37]. Thus there is a need for studies which use objective measures of physical activity as an important indicator of functional ability. Currently, habitual physical activity levels in large scale studies of healthy adult populations are most commonly objectively measured through the use of accelerometers [38].

Only nine studies since 2002 have used accelerometry as a measure of physical function in patients before and after TKA [39], some reporting little or no change in physical activity after surgery [24, 26, 33, 40] and others showing improvements in self-report measured functional ability [41, 42]. The variability in devices used to assess habitual physical activity before and after TKA makes the comparison of results across studies difficult. However, the ActiGraph GT1M accelerometer (an earlier version of the ActiGraph) has been used to assess the intensity and amount of physical activity occurring following TKA [26] but very small changes in activity were found. In addition, the timing and length of activity assessment is an important factor in determining changes in physical function in studies of TKA with some objectively measured studies showing improvements in physical activity six months after TKA [24, 43], and others showing very little or no improvement in daily activity at three or six months post-surgery [26, 41].

Recently, opportunities for measuring patterns of sitting and lying time have been made possible through the use of inclinometers e.g. the activPAL (PAL technologies Ltd, Glasgow, UK). The activPAL produces highly accurate and precise estimates of total sedentary time in free-living individuals [44] and has been validated to estimate time in different postures, step count, static and dynamic behaviours and sit-to-stand transitions in laboratory studies [44–46]. Only one study has used the activPAL in a cross-sectional assessment of energy expenditure in knee OA patients prior to arthroplasty [47]. The use of the activPAL to measure sedentary behaviour following TKA has not been done before.

The objective assessment of habitual physical activity may provide an alternative method of assessing whether functional ability is improved in OA patients following TKA, as a change in activities of daily living (assessed using sedentary behaviour and light activity measurements) without a change in moderate to vigorous physical activity may correspond to a patient's improved ability to function. Thus the aims of this study are to 1) describe habitual physical activity and sedentary behaviour patterns in knee OA patients scheduled for TKA, 2) to investigate the effects of unilateral primary TKA on objectively and subjectively measured habitual physical activity, sedentary behaviour and health outcomes of patients with knee OA and 3) to determine whether subjective measures of functional ability and sedentary behaviour (questionnaires) are correlated with objective measures of habitual physical activity and sedentary behaviour (accelerometry) before and after TKA. These data will help inform targeted interventions for the improvement and maintenance of physical activity.

Methods

Study participants

The study population will include all knee osteoarthritis patients receiving care at the Charlotte Maxeke Johannesburg Academic Hospital. Patients will be recruited from the Orthopaedic Division of the hospital. The participants for this study will be knee OA patients scheduled (on surgical waiting list) for a single primary total knee artheoplasty or replacement surgery. Knee OA will be diagnosed based on clinical criteria as defined by the American Rheumatism Association (ACR) [48]. Prospective participants will be given an information sheet describing the study and will have the study verbally explained to them prior to participation in the study. Participants will be required to sign a consent form should they wish to participate in the study. Participants will then complete a general health questionnaire in order to confirm eligibility in the study. Patients will be recruited to participate in the study if they have been diagnosed with knee OA and attended to by surgeons in the Orthopaedic Surgery Unit at the Hospital. Potential participants will be eligible to participate in the study by the attending orthopaedic surgeon. They will also be included if they have been refractory to analgesics for at least six months, are male or female between 55 and 80 years of age, are undergoing primary unilateral TKA surgery and are ambulant with or without assistive devices.

Patients will be excluded from participating in the study if they use assistive ambulatory devices for mobility problems other than knee OA, are scheduled for bilateral knee arthroplasty, a second knee arthroplasty or revision, or are scheduled for total hip replacement, or if they have co-morbidities or medical conditions that affect physical activity such as congestive heart failure, stroke and other neurological problems, chronic obstructive pulmonary disease (COPD), gout and/or sepsis, have been diagnosed with arthritis other than osteoarthritis (according to the 1987 American College of Rheumatology (ACR) criteria [48]), if further joint surgery is anticipated within six months of the index knee replacement or are non-ambulant or wheel chair-bound.

Study site

The study will be conducted at the Charlotte Maxeke Academic Hospital in Johannesburg, South Africa. It is an accredited central hospital with about 1088 beds serving patients from across Gauteng and neighbouring provinces. The hospital is situated in Parktown and also, serves as the main teaching hospital for the Faculty of Health Sciences, University of the Witwatersrand. Study participants will be recruited from the Division of Orthopaedics in the hospital. This hospital is chosen because: (1) it is a tertiary hospital that runs several specialist clinics including the Orthopaedic Division where TKA among several other surgeries are performed and (2) there is a collaboration between the Academic staff of the Faculty of Health Sciences of University of the Witwatersrand and the hospital Staff for teaching and research which will facilitate accessibility to patients.

Study design

This a longitudinal follow-up study of a cohort of participants who have been diagnosed with knee osteoarthritis and who are scheduled for TKA. After enrolment into the study, baseline assessments will be done prior to TKA. After TKA, participants will be followed-up and the same assessments done at baseline will also be done at six weeks, and six months post-operatively (Fig. 1). Habitual physical activity and sedentary behaviour will be measured using accelerometry (Actigraph GTX3+ and ActivPal monitors) at the specific time points. In addition, general health, functional ability, generic quality of life and pain questionnaires will be conducted at each time point on each participant.

Trial registration

This trial has been registered with the ClinicalTrials.gov registry (trial registration number: NCT02675062).

Outcomes

All outcomes will be measured at baseline, six weeks after surgery and again six months after the surgical intervention (Table 1). The primary outcomes of this study will be an improvement habitual physical activity and a reduction in sedentary time after TKA. The secondary outcomes will be improvements in osteoarthritis-specific quality of life measures: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), knee related quality of life from Knee injury and Osteoarthritis Outcome Score (KOOS), Knee Society Clinical Rating System (KSS), the Oxford Knee Score (OKS), self reported activity using the UCLA activity index; subjective pain scores, and self reported sleep quality.

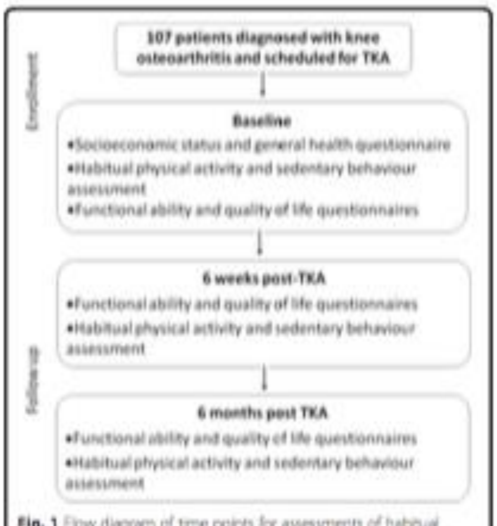

Fig. 1 Flow diagram of time points for assessments of habitual physical activity, sedentary behaviour, functional ability, quality of life, general health, mobility and pain questionnaires before and after total knee arthroplasty (TKA)

Sample size determination

Time spent in bouts of sedentary activity longer than 20 min is associated with poorer health outcomes [49]. In order to achieve a 2 % (which, for an average 16 h day, equates to a 20 min) reduction in the time spent in sedentary behaviour per day [26], a total sample of 107 participants will be required in this study to detect a significant effect of knee arthroplasty on sedentary behaviour (power of 80 %).

Questionnaires

Socioeconomic Status (SES) and General Health Questionnaire (GHQ)

Socioeconomic status (SES) will be determined using a household amenity questionnaire [50]. Eligibility into the study will be determined using a GHQ in order to determine whether participants have any comorbidities that might exclude them from participation. Furthermore the GHQ will be used to record the health demographics of the participants, such as history of knee OA and medication use. The SES and general health questionnaires will be completed at the first visit only.

Functional ability questionnaires

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) WOMAC assesses pain, stiffness, and physical function in patients with hip and knee OA (Bellamy, 2002). WOMAC consists of 24 items divided into 3 subscales: (1) 5 Pain items for assessing pain (2) 2 Stiffness items and (3) 17 Physical Function items. Each of the items requires the respondent to answer questions on 5-point Likert scale. 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 items are summed and transformed to a 0-100 scale. Higher scores indicate improved pain, stiffness and physical function. Thus, a score of 0 represent the worst

Table 1 Summary of outcome measures and respective collection method

Outcome	Variables	Measurement method	Time points (months)
Primary	Habitual physical activity	Accelerometry (ActiGraph worn on the hip)	0, 1.5, 6
	Sedentary behaviour	Accelerometry (activPAL worn on thigh)	0, 1.5, 6
Secondary	Knee OA-specific functional ability and quality of life	WOMAC	0, 1.5, 6
		KOOS	
		KSS	
		OKS	
	Activity	UCLA activity index	0, 1.5, 6
	Pain	VAS	0, 1.5, 6
	Sleep quality	Sleep questionnaire	0, 1.5, 6

possible state while a score of 100 represents the best possible state.

Knee Injury and Osteoarthritis Outcome Score (KOOS) The KOOS consists of 5 subscales: Pain, other symptoms, function in daily living, function in sport and recreation and knee-related quality of life. The previous week is the time period considered when answering the questions. Standardized answer options are given on five (5) Likert scales and each question is assigned a score from 0 to 4. The score is a percentage score from 0 to 100, with 0 representing extreme symptoms/problems and 100 representing no problems. The KOOS has been used in previous studies for evaluating outcome after TKA [51, 52].

Knee Society Clinical Rating System Score (KSS) The Knee Society Clinical Rating System is a rating system which consists of two scores: knee and patient functional scores. Both scores range from 0 (worst health or functioning) to 100 (best health or functioning). This instrument has been used for tracking and reporting outcomes after total and partial knee arthroplasty worldwide [53]. Fifty of 100 points in the knee score are allocated to pain assessment with 50 representing no pain whereas the other 50 points are allocated for a clinical assessment with 50 representing at least 0°-125°of knee flexion with no active lag, no instability and normal alignment. The function score reflects patient-reported walking distance and stair-climbing and makes deductions for use of a walking aid, with 100 representing unlimited walking distance and normal stair-climbing without use of an aid [54].

Oxford knee score (OKS) The OKS consists of 12 questions assessing pain and physical disability using a 5-point Likert scale and it generates a single score ranging from 0 (worst functional outcome) to 100 (best functional outcome) [55].

Physical activity questionnaire

The UCLA activity index is a scale from 1 to 10 with phrases ("no physical activity" to "regular participation in impact sports") which the patient chooses to best describe their most appropriate activity level. The UCLA has been shown to be the most appropriate subjective physical activity assessment for patients undergoing joint arthroplasty [56].

Pain and sleep questionnaires

Joint pain, sleep quality and morning vigilance at each time point of the study will be assessed on a 100-mm visual analogue scale (VAS). The pain and sleep questionnaires will be administered at each visit to the hospital. All questionnaires have been previously validated.

Anthropometric measurements

Height will be measured to the nearest millimetre with the participants bare foot using a stadiometer (Seca, model 202, Germany). Weight will be measured to the nearest gram using a scale (Mettler, Model TE120 ME36400, Switzerland) with the participants bare foot and wearing light clothing. Body mass index (BMI) will be calculated from the height and the weight (weight/square of height) for each participant.

Physical activity and sedentary behaviour measurements

ActiGraph GT3X+ Accelerometer

The ActiGraph GT3X+ is a small (4.6 cm × 3.3 cm × 1.5 cm) lightweight (19 g) tri-axial activity monitor that provides data on physical activity including activity counts, energy expenditure (kcal), steps and activity intensity (METs). The GT3X+ has an inclinometer to determine body position in sitting, lying and standing. The ActiGraph GT3X+ will be worn by participants for 24 h/day for seven days at each of the assessment time points. It will be attached to an elastic nylon strap which the participants can wear as a belt around the waist on the side of the affected knee. Participants will be asked to remove the ActiGraph when showering, bathing or swimming. After seven days of accelerometer wear, the accelerometers will be collected at the next possible visit to the hospital or arrangement will be made for collection from participants at a location most convenient to them.

The data will be downloaded and processed using a custom built SAS program (v 9.3, SAS Institute, Cary, NC, USA) that implements a series of decision rules with user-modifiable thresholds to automatically identify waking wear data for continuously worn ActiGraph GT3X+ of 60 s epoch vertical axis data. Non-wear time will be classified as one minute intervals with consecutive zero counts for a minimum of 90 min (with an allowance of up to 3 min of counts between 0 and 50). For the day to be classified as valid, a minimum wear time of 10 h (600 min) is required. Each 60 s epoch of accelerometry data is classified according to calibration equations as sedentary if <100 counts per minute (cpm) [57], light intensity activity if between 100 and 1951 cpm, moderate-vigorous intensity activity if between 1952 and 5724 cpm and vigorous if >5724 cpm [58]. Adjacent epochs within the same intensity will be grouped into bouts. Only participants with four or more valid days of wear (including at least one weekend day) will be included in the analyses. Total daily time spent in the different PA intensities will be obtained by totalling the duration of all the bouts at each level for each day. The values will then be normalised to total wear time and averaged over the number of valid days to derive an estimate of the mean time spent within each intensity. A break in sedentary time will be counted as one minute or more where the counts per minute is greater than 100.

activPAL accelerometer

The activPAL is a small (2.0x1.4x0.3 in.) and light (20.1 g) single-unit accelerometer device worn on the mid-thigh fastened and secured by a non- allergenic adhesive tape and uses accelerometer-derived information about thigh position to estimate time spent in different body positions in lying, sitting and standing in 15 s epochs [44]. An activPAL will be taped to the thigh of the patient with waterproof taping and the patient will be asked to keep the activPAL on for the same amount of time as the ActiGraph. The activPAL can be covered with waterproof taping therefore, there will be no need to remove the activPAL when showering, bathing or swimming and therefore unless the device is reported to have fallen off by the patient, there will be no need for non-wear time classification for the activPAL data. The activPAL will be collected at the same time as the ActiGraph and data will be downloaded and analysed. The data are recorded in 15 s epochs and the manufacturer's software will be used to determine the variables of interest from the downloaded activPAL data which will include the start time and duration of each sitting, lying, standing and stepping bout. Total sedentary time will be determined by summing the duration of all sitting/lying bouts. The interruption or break from sedentary time will be indicated at points where a sitting/lying bout is followed by a standing or stepping bout. Because the activPAL is worn for the same period as the ActiGraph, the same periods of sleep that are removed from the ActiGraph data, will also be removed from the activPAL data to be analysed. Further time-intensive methods of analysis will be employed according to current best practice guidelines [59].

Data analyses

Socioeconomic data will be summarised by descriptive statistics. Also, means and standard deviations will be used to summarise data for age, anthropometric (height, weight, BMI and %body fat), ActiGraph GT3X+ and ActivPAL.Scores for WOMAC, KOOS, OKS and KSS will be calculated by their respective scoring systems. Data will be analysed using SPSS v20 (SPSS Inc., Chicago, IL, USA).

Linear mixed models will be used to determine relationships between objectively measured habitual physical activity and sedentary behaviour, functional capacity and quality of life between pre-operative and 6 weeks and 6 months post-operatively. The model will be used to compare subjective measures of functional mobility (questionnaires) with objective measure of habitual physical activity. A multiple regression analysis will be used to describe the association between physical activity and/or sedentary behaviour, functional capacity and quality of life of OA patients before and after TKA. Also, a multiple regression will be used to determine the relationship between habitual physical activity and sedentary behaviour on anthropometric parameters of OA patients before and after TKA. A p-value of less than 0.05 will be considered significant.

Discussion

The present study will contribute to the field of musculoskeletal health by providing a rich detailed description of the patterns of accumulation of physical activity and sedentary behaviour in patients with knee OA. These data will contribute to existing knowledge using an objective measurement for the assessment of functional ability after total knee replacement surgery. Although studies have used accelerometry to measure physical activity in knee OA patients, the data provided thus far have not delved into the detailed patterns of how and when the entire spectrum of physical activity is accumulated before and after TKA. Accurate assessment of physical activity is important for physical activity interventions that target special populations.

A key advantage of this study over previous studies includes the use of more than one monitor to objectively assess physical activity and sedentary behaviour. The activPAL may be used to capture the energy expenditure of habitual physical activity, however the real value of the tool is its ability to assess sedentary behaviour in terms of postural changes (lying/sitting). Furthermore, the way we wish to obtain a richer set of metrics to describe patterns and accumulation of physical activity is rather more than the activPAL is able to provide, hence the reason why both monitors will be used in this study. Detailed postural classifications of how patients with knee OA spend their time prior to and after surgery will be of interest to health care providers. An increase in sedentary behaviour leads to an increased risk of sarcopenia in healthy elderly populations [60]. The muscle degeneration that is associated with sedentary behaviour in an ageing population has implications for patients with knee OA, as the immobility and reduced functionality may be exacerbated by the knee OA. Furthermore greater levels of sedentary behaviour may occur at an earlier age in patients with knee OA predisposing these patients to an increased risk of sarcopenia as they age. No studies that we are aware of have investigated sedentary behaviour patterns (using the activPAL) in patients with knee OA therefore comprehensive measurement on patterns of sedentary behaviour in this population is needed to implement effective interventions aimed at decreasing sedentary behaviour levels.

Additionally, there are no data on objectively measured habitual physical activity or sedentary behaviour before and after total knee replacement on South African patients. Surgical intervention may be considered at an earlier stage of the disease in developed countries, compared to low to middle income countries such as South Africa where surgical intervention may often be delayed due to long waiting lists and budgetary constraints. Knowing more detailed information about how patterns of physical activity and sedentary time may change following surgical intervention will help inform best practices by providing clear information about whether patients can expect to improve their physical activity levels and decrease their time spent in sedentary behaviours by enough time so as to reduce their risk of cardiometabolic disease (which is a risk associated with a lack of activity). Describing changes in daily patterns of activity and sedentary behaviour may allow for further studies to target the timing and duration of physical activity interventions on a daily basis in order to attempt to increase the amount of physical activity patients with knee OA take part in.

As global populations age and in order to decrease the burden of the disease, there will be an increasing need for total knee replacements in adults affected by knee OA. This study will investigate the patterns by which habitual physical activity and sedentary behaviour are accumulated in patients with knee OA before and after surgery, and will therefore assist in informing targeting interventions to improve patterns of physical activity. Furthermore, a change in exercise guidelines from increasing the volume of exercise to offsetting the time spent in deleterious behaviours such as excessive time spent sitting, may contribute to developing more relevant criteria for physical activity prescription in patients with osteoarthritis.

Abbreviations

KOOS, Knee Injury and Osteoarthritis Outcome Score; KSS, Knee Society Clinical Rating System; METS, metabolic equivalents; OA, osteoarthritis; OKS, Oxford Knee Score; PA, physical activity; SB, sedentary behaviour; SES, socioeconomic status; TKA, total knee arthroplasty; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

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Availability of data and material

Not applicable.

Authors' contributions

RM Conceptualization of study, development of study design, writing of drafts, editing of drafts. EF Development of study design, writing of drafts, editing of drafts. LM Development of study design, editing of drafts. JP Development of study design, editing of drafts. DVDJ Conceptualisation of study, development of study design, editing of drafts. MT Conceptualization of study, development of study design, editing of drafts. JMCV Conceptualization of study, development of study design, writing of drafts, editing of drafts. All authors have read and approved the final version of the manuscript.

Authors' information

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

Ethical approval has been obtained from the Health Research Ethics Committee (HREC) of the University of the Witwatersrand (ethics clearance number M150323). An informed written consent will be obtained from participants after explaining the protocol to them before participating in the study. The data gathered from participants will be kept anonymous and will be used only for the purpose of the study.

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APPENDIX K – Peer-reviewed journal article 2

Journal of Aging and Physical Activity

Sedentary Behaviour in Patients with Knee Osteoarthritis before and after Total Knee Arthroplasty: A Systematic Review

Journal:	*Journal of Aging and Physical Activity*
Manuscript ID	JAPA.2017-0214.R1
Manuscript Type:	Scholarly Review
Focus Area:	arthritis < clinical populations, exercise physiology, Other
Statistical Methods:	Other, Systematic review
Free-Form Keywords:	Physical activity, Sedentary behaviour, Older adults, knee replacement

Human Kinetics, 1607 N Market St, Champaign, IL 61825

Sedentary Behaviour in Patients with Knee Osteoarthritis before and after Total Knee Arthroplasty: A Systematic Review

Abstract

Objective: The objective of this systematic review is to integrate the available evidence on changes in sedentary behaviour (SB) in patients with knee osteoarthritis (OA) after total knee arthroplasty (TKA). **Methods:** A systematic literature search from January 2002 to 31 October 2017 was performed for studies assessing objectively and/or subjectively measured SB following TKA. The Scottish Intercollegiate Guidelines Network (SIGN) Methodology appraisal tool was used to critically appraise the methodological quality of the included studies. **Results:** Ten studies reporting on SB with a total of 1,028 participants were included in the review. Three studies reported changes in SB with two showing a reduction in SB and one (with high risk of bias) an increase in SB after TKA. Seven studies showed no change in SB following TKA. **Conclusion:** Currently there is insufficient evidence which suggests that SB time improves following TKA. Detailed assessments of SB after TKA are needed.

Keywords: sedentary behaviour, physical activity, total knee arthroplasty, knee osteoarthritis, systematic review

APPENDIX L – Peer-reviewed journal article 3

Knee Surgery, Sports Traumatology, Arthroscopy
https://doi.org/10.1007/s00167-018-4987-2

KNEE

Light intensity physical activity increases and sedentary behavior decreases following total knee arthroplasty in patients with osteoarthritis

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Abstract

Purpose To describe objectively measured changes in the volume and pattern of physical activity and sedentary behavior in patients undergoing total knee arthroplasty for osteoarthritis.

Methods Physical activity and sedentary behavior were measured in patients (13 males, 76 females) with a mean age of 64 years (range 55–80) and end-stage osteoarthritis of the knee, using an accelerometer (ActiGraph GT3X+) for seven consecutive days (24 h/day) prior to, 6 weeks and 6 months after total knee arthroplasty. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), University of California Los Angeles (UCLA) Activity index and range of motion (ROM) were also assessed.

Results Proportion of time spent in sedentary behavior decreased from baseline to 6 months (mean 70.1 vs. 64.0%; $p=0.009$) and the interruptions to sedentary behavior improved between baseline and 6 months after total knee arthroplasty (mean 85.0–93.0 breaks/day, $p=0.014$). Proportion of time spent in light physical activity increased from baseline to 6 months after total knee arthroplasty (29.0 vs. 34.8%; $p=0.008$). There was no change in time spent in moderate to vigorous physical activity after total knee arthroplasty. WOMAC (median 71.0 vs. 4.0, $p<0.001$), UCLA (median 2.0 vs. 5.0, $p<0.001$) as well as ROM [median (0.0°–90.0°) vs. (0.0°–110°), $p<0.05$] scores improved between baseline and 6 months after total knee arthroplasty.

Conclusion Clinically, functional improvements in patients following total knee arthroplasty may be assessed by objectively measuring changes in low intensity activity behaviors. The use of accelerometers in this study gives new insights into activity accumulation patterns in a clinical population and highlights their use in determining a behavioral response to an intervention.

Level of evidence II.

Keywords Physical activity · Sedentary behavior · Accelerometry · Knee osteoarthritis · Total knee arthroplasty

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Introduction

Knee osteoarthritis (OA) is associated with decreased physical functional ability, poor quality of life, decreased physical activity and increased time spent in sedentary behavior [13, 23, 40]. Based on self-report data and a few studies which have objectively measured activity behaviors, the majority of patients with knee OA are physically inactive [19, 40], that is, they do not accumulate enough moderate and vigorous physical activity (MVPA) to meet the current physical activity guidelines of at least 150 min of MVPA per week [32].

The most definitive and cost-effective treatment for advanced knee OA is total knee arthroplasty (TKA) [33]. The primary aim of TKA is to treat pain and improve functional

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ability and health-related quality of life [20]. Despite substantial improvements in the patient-reported outcome measures (PROMs) for pain, physical activity, functional performance and quality of life following TKA, some studies report improvements in physical activity and/or sedentary behavior [7, 24, 39], while others show no improvements [15, 18, 38]. A recent systematic review concluded that no change in objectively measured physical activity occurs 6 months after TKA [17].

The apparent contradiction in improvements between objectively measured activity behaviors and PROMs suggest that despite patients reporting improvements in function, surgery may not be effective for improving the total volume of physical activity in patients with end-stage knee OA. Nonetheless, there may be subtleties in the way objective measures of physical activity and sedentary behavior change after TKA that have not been previously described. For example, in addition to low physical activity levels in knee OA patients, the related and yet discrete importance of prolonged periods of inactivity and absence of whole body movement in people with knee OA is becoming increasingly recognized [41]. A few studies have assessed sedentary behavior with physical activity in patients undergoing TKA [15, 18, 24, 38, 41] but none have considered and described the detailed daily patterns of accumulation of both physical activity and sedentary behavior following TKA. An understanding of these patterns may be useful to inform clinicians (1) as to whether the data obtained objectively can provide insight into behavioral responses to TKA, (2) as to whether objective data are useful in their ability to determine the effect of interventions such as TKA and (3) for the development of targeted interventions for improving physical activity and decreasing time spent sedentary postoperatively. With technology, such as accelerometry, that is now available to measure detailed outcomes of the whole spectrum of daily activity behaviors (from sedentary to light to vigorous intensities), studies that harness the detail of these activity behavior data are needed to determine if, when and how patients may change their activity behaviors after undergoing TKA. In the current study, it was hypothesized that overall volume of activity behaviors would not change following TKA; however, the patterns of accumulation of those activity behaviors would change. The primary objective of this study was to describe changes in both the volume and patterns of activity behaviors (PA and SB) using accelerometry in patients undergoing TKA. A secondary objective was to assess changes in PROMs following TKA.

Materials and methods

Patients with advanced knee OA, scheduled for primary TKA at a tertiary hospital in South Africa took part in this study. The patients were recruited and followed up from August 2015 to April 2017. Inclusion criteria for the study were patients who: (1) were between the ages of 55 and 80 years, (2) met the 1986 American Rheumatology Association (ACR) criteria for knee OA [1], (3) had Kellgren and Lawrence grade 3 or 4 radiographic changes [22], (4) were refractory to conservative medical therapy for at least 6 months, (5) were undergoing primary unilateral TKA surgery and (6) were ambulant with or without assistive devices.

Exclusion criteria were: (1) patients having any other form of chronic arthritis [e.g., rheumatoid arthritis (RA)], (2) significant symptomatic chronic OA of the contralateral knee and/or hip, and (3) having co-morbidities or medical conditions that affect PA such as congestive heart failure, neurological problems (such as stroke) and chronic obstructive pulmonary disease (COPD) as determined using a general health questionnaire (GHQ) [29].

The Human Research Ethics Committee of the University of the Witwatersrand approved the study (clearance number: M150323). Written informed consent was obtained from all patients. The study has also been registered on the ClinicalTrials.gov database (Trial reg. no: NCT02675062-4 February 2016).

Study design

This study was a longitudinal observational design and the details of the study protocol have been previously published [29]. Baseline assessments were done 2 weeks prior to TKA, with patients being off prescription pain medication for at least a week. All patients were implanted with cemented posterior stabilized knee prosthesis (Genesis II, Smith and Nephew, Durban, South Africa). Patients underwent standard physiotherapy care after the surgery. Postoperatively, patients were followed up at 6 weeks and 6 months. Briefly, the data that were collected included patient demographics and anthropometrics, self-reported physical function and health-related quality of life, range of motion (ROM) and PA and SB. The assessment time points corresponded to the required appointments for patients to consult with their surgeons.

Patient-reported outcome measures

A general health questionnaire (GHQ) was used to determine the eligibility for the study by obtaining information on health history, history of knee OA, history of medication and smoking, previous or scheduled surgery other than TKA and present or absence of any co-morbidities (not limited to hypertension, diabetes mellitus, high cholesterol, chronic obstructive pulmonary disorders, heart disease and stroke). The socioeconomic status (SES) was determined using a household amenity and education questionnaire (HAQ) [6].

The University of California, Los Angeles (UCLA) activity index was used to assess the self-reported activity level of patients [18].

The Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index was used to assess pain, stiffness and physical function in patients at each timepoint [4].

Anthropometric and range of motion (ROM) measurements

Height was measured to the nearest meter with the patients shoeless using a stadiometer (Seca, model 202, Germany). Weight was measured to the nearest 0.1 kilograms using a scale (Mettler, Model TE120 ME36400, Switzerland) with the patients shoeless and wearing light clothing. Active flexion and extension ROMs of the affected knee were measured using a plastic goniometer.

Objective measurement of physical activity and sedentary behavior

Physical activity and sedentary behavior were objectively measured using a continuous wear (24 h/day) protocol over a 7-day period with the Actigraph GT3X + accelerometer (Actigraph, LLC, Fort Walton Beach, FL, USA). The GT3X + was programmed to record raw data at a frequency of 30 Hz which were later reduced to vertical axis movement counts per 60 s epoch for the purpose of the current analyses. The ActiGraph was attached to an elastic belt, which the patients wore around their waist on the same side of the affected knee. Patients wore the accelerometer for seven consecutive days and the ActiGraph was collected at the next possible visit to the hospital or arrangements were made for collection from patients at a location most convenient to them. The patients were instructed to remove the ActiGraph when showering, bathing or swimming.

The data were downloaded and reduced using a custom built SAS program (v 9.3, SAS Institute, Cary, NC, USA). Sleep periods were either calculated using a validated algorithm [27] or, where distinct sleep times could not be obtained, sleep periods were determined by visual inspection and confirmed from the patient-reported sleep and wake times recorded on the general health questionnaire. Non-wear time was classified as 1 min intervals with consecutive zero counts for a minimum of 90 min (with an allowance of up to 3 min of counts between 0 and 50) [10]. 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 h (600 min) was required. Only patients with four or more valid days of wear time were included for data analyses. Common cut points were used to classify each minute as sedentary (< 100 counts per minute, cpm) [25], light intensity (100–1951 cpm), moderate intensity (1952–5724 cpm), or vigorous intensity (> 5724 cpm) [14]. Total volumes of activity in the different intensities (sedentary, light and moderate vigorous) as well as patterns of activity (i.e., bouts of time spent in each activity intensity) were the variables that were extracted from the waking wear data.

Statistical analysis

The data were analyzed using SPSS (version 24, SPSS Inc., Chicago, IL, USA). All patients with at least four valid days of ActiGraph data at baseline and/or 6 weeks and 6 months after TKA were included in the analysis. However, patient characteristics (anthropometric, general health and socioeconomic data) were reported for all those recruited into the study using descriptive statistics (mean and standard deviation or median and interquartile range or percentages). The amounts of time spent in SB, light physical activity (LPA) and MVPA at baseline and at 6 weeks and 6 months after TKA were presented descriptively (using means and 95% confidence intervals or median and interquartile range). SB and LPA data (which were normally distributed, assessed by Shapiro–Wilks test) between baseline and 6 weeks and 6 months after TKA were compared using a linear mixed model, whereas a generalized linear model was used for MVPA time and the percentages of awake wear times spent in each of the activity behaviors (not normally distributed). Fixed effect used in the models was time and the random effect was subjects. The variance–covariance structures were selected based on Bayes Information Criterion and the unstructured variance–covariance was used. Patients' age, BMI and awake wear times were included in the models as known covariates. Accumulation of activity across categories of intensity and bout duration was also described using exposure variation analysis (EVA) [34]. The hourly variations of the sedentary to light activity ratios were analyzed using a generalized linear model with hour of the day and assessment time points as factors.

Scores for UCLA and WOMAC (calculated by the scoring system) were reported descriptively (with median and interquartile range). Questionnaire scores between baseline, 6 weeks and 6 months after TKA were compared using a generalized linear model. A p value of less than 0.05 was considered significant. An a priori sample size calculation indicated that a minimum sample size of 107, including a 20% drop out rate to follow-up, was required to achieve 2% reduction in sedentary time with a power of 80% [29].

Results

A total of 89 (76 female; 13 male) patients with mean (SD) age of 64.8 (8.7) years ranging from 55 to 80 years and BMI of 34.0 (7.7) kg/m^2 were recruited into the study. Figure 1 is a flow chart showing the total number of patients recruited into the study at baseline and the drop outs to follow-up. Only 73 patients underwent the TKA surgery, while the remaining 15 patients had their surgeries suspended on account of unsatisfactory clinical reports ($n=14$) and one patient declined to undergo the surgery due to family issues. A further 16 patients were lost to follow-up: six dropped out at 6 weeks post-TKA (three travelled out of Johannesburg, two could not be reached and one opted to continue treatment at a private clinic); and ten dropped out at 6 month post-TKA (four travelled out of Johannesburg, three declined to continue the study, two lost their monitors and one had a faulty monitor).

Table 1 shows the patients characteristics for those who (1) underwent TKA surgery; (2) completed the study 6 months after TKA and (3) had valid or insufficient ActiGraph GT3X + activity data at 6 months after TKA.

Patient and physician-reported outcomes before and after TKA

Self-reported PA was significantly higher at 6 weeks ($p<0.001$) and 6 months ($p<0.001$) after TKA compared to baseline (Table 2). Patients reported no pain and stiffness 6 months after TKA compared to baseline ($p<0.001$).

Both the flexion and extension ranges of motion (ROM) improved significantly 6 months after TKA ($p<0.001$ and $p=0.028$, respectively).

Changes in volume of activity behaviors pre and postoperatively

Table 3 shows the comparisons of total volume and patterns of PA and SB of patients before and after TKA. The number of valid days of ActiGraph wear, total awake wear time per day and total activity counts per day and per minute for all awake wear time was not different between baseline and 6 weeks and 6 months after TKA.

The percentage of awake wear time spent in SB ($p=0.009$) as well as the overall daily sedentary time ($p=0.03$) decreased significantly from baseline to 6 months after TKA. The total number of breaks from SB significantly increased at 6 months after TKA compared to 6 weeks after TKA ($p<0.001$) and baseline ($p=0.022$). The duration of breaks from SB was lower

Fig. 1 Flow chart illustrating patient recruitment from baseline to 6 month follow-up

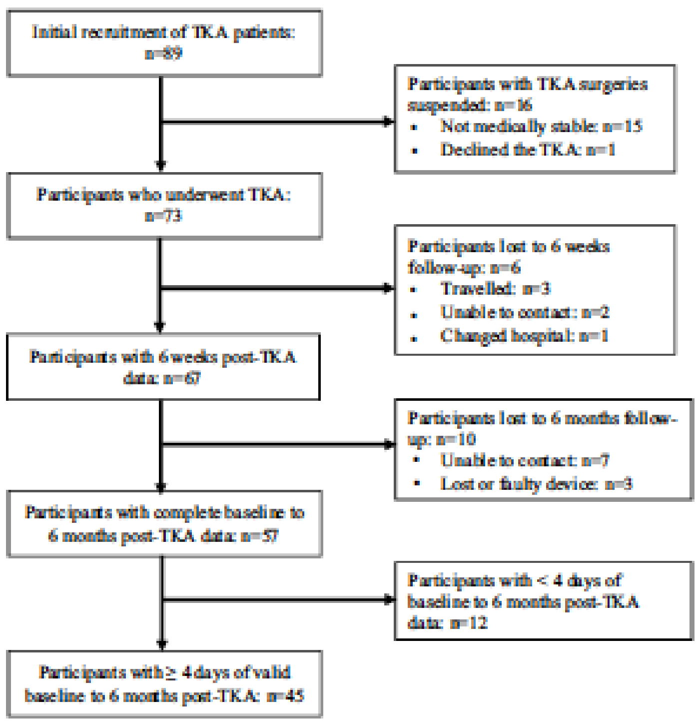

Table 1 Characteristics of patients who underwent TKA, those who completed the follow-up and those who completed the follow-up with and without valid ActiGraph data

	Patients who underwent TKA ($n = 73$)	Patients with complete 6 months follow-up data ($n = 57$)	Patients with complete 6 months and valid ActiGraph data ($n = 45$)	Patients with complete 6 months and insufficient ActiGraph data ($n = 12$)
Age (years)	64.0 (8.7)	64.2 (9.0)	63.8 (8.8)	64.3 (9.4)
Gender, *n* (%)				
Females	67 (92)	53 (93)	42 (93)	12 (100)
Males	6 (8)	4 (7)	3 (7)	0 (0)
Race, *n* (%)				
Black	53 (73)	41 (72)	33 (73)	11 (92)
Caucasian	20 (27)	16 (28)	12 (27)	1 (8)
Weight (kg)	84.8 (20.0)	84.3 (20.8)	84.6 (21.0)	87.3 (17.5)
Height (m)	1.6 (0.1)	1.6 (0.1)	1.6 (0.1)	1.6 (0.1)
Body mass index (kg/m^2)	34.2 (7.5)	34.3 (7.9)	34.6 (7.8)	36.6 (7.6)
LHS, median (IQR), (days)	7.0 (3)	7.0 (3)	7.0 (3)	7.0 (5.0)
Side of TKA, *n* (%)				
Left	30 (41)	24 (42)	19 (42)	6 (50)
Right	43 (59)	33 (58)	26 (58)	6 (50)
Smoking (yes), *n* (%)	6 (8)	4 (7)	3 (7)	3 (7)
Diabetes mellitus (yes), *n* (%)	8 (11)	5 (9)	5 (11)	1 (8)
Hypertension (yes), *n* (%)	37 (51)	28 (49)	22 (49)	6 (50)
Dyslipidaemia (yes), *n* (%)	7 (10)	6 (11)	2 (5)	2 (17)
Educational status, *n* (%)				
Below high school	24 (33)	20 (35)	18 (40)	4 (33)
High school complete	37 (51)	30 (53)	20 (44)	7 (58)
Tertiary level complete	12 (16)	7 (12)	7 (16)	1 (9)
SES score	9.9 (2.8)	10.0 (2.9)	9.9 (3.1)	9.7 (3.1)

Age, weight, height, body mass index and SES score are presented as mean (SD), whereas length of hospital stay is presented as median (interquartile range, IQR). The remaining data are presented as frequencies (%)

LHS length of hospital stay, *SES* socioeconomic status, *TKA* total knee arthroplasty

Table 2 Comparisons of patient and physician-reported outcomes before and after TKA

	Baseline ($n = 79$)	6 weeks after TKA ($n = 62$)	6 months after TKA ($n = 45$)	Main effect p value	p value*
UCLA score	2.0 (1.0)	3.5 (1.0)	5.0 (1.0)	<0.001	<0.001
WOMAC scores					
Total score	71.0 (27.0)	22.5 (19.0)	4.0 (11.3)	<0.001	<0.001
Pain	15.0 (6.0)	3.0 (5.0)	0.0 (2.0)	<0.001	<0.001
Stiffness	6.0 (2.0)	2.0 (1.0)	0.0 (2.0)	<0.001	<0.001
ADL	51.0 (17.0)	16.5 (17.0)	3.5 (9.0)	<0.001	<0.001
ROM					
Flexion (°)	90.0 (10.0)	95.0 (10.0)	110.0 (15.0)	<0.001	<0.001
Extension (°)	0.0 (6.0)	0.0 (4.0)	0.0 (0.0)	0.01	0.012

Data are presented as median (interquartile range). A higher score for WOMAC pain, stiffness and ADL subscales (maximum scores possible were 20, 8, and 68, respectively) indicates a worse outcome. The highest possible score for UCLA is 10, indicating regular participation in impact sports. Normal ROM is 0°–140°; however, ROM of 0°–110° (i.e., 0° extension and 110° flexion) after TKA indicates a good result

*p value calculated between baseline and 6 months after TKA (Bonferroni)

Table 3 Comparisons of volume of activity behaviors before and after total knee arthroplasty

	Baseline ($n = 79$)	6 weeks after TKA ($n = 62$)	6 months after TKA ($n = 45$)	Main effect p value	p value*
Valid days	5.7 (5.5–5.9)	6.0 (5.8–6.3)	6.0 (5.7–6.3)	0.067	n.s
Waking wear time (min/day)	927.0 (903.2–956.7)	901.7 (874.4–929.0)	927.8 (901.7–953.8)	0.126	n.s
Activity counts, all awake wear time (counts/day)	162,018 (133,675–190,361)	132,094 (109,961–154,227)	196,751 (165,206–228,296)	<0.001	n.s
Activity counts, all awake wear time (counts/min)	170 (143–198)	145 (123–168)	209 (177–242)	0.001	n.s
Sedentary behavior (SB)					
Sedentary time, % awake wear[a]	70.1 (67.5–72.7)	72.0 (69.5–74.9)	64.0 (60.6–67.9)	0.001	0.009
Sedentary time (min/day)	649.7 (622.0–677.3)	649.1 (617.1–681.1)	594.0 (555.9–632.0)	0.033	0.030
Breaks from SB (number/day)	85.2 (80.4–90.1)	82.2 (76.8–87.6)	93.0 (88.1–97.9)	<0.001	0.022
Duration of break from SB (min/break)	3.2 (3.0–3.5)	3.0 (2.7–3.3)	3.7 (3.2–4.0)	0.010	n.s
Light physical activity (LPA)					
Light physical activity, % awake wear[a]	29.0 (26.6–31.4)	27.4 (24.7–30.0)	34.8 (31.3–38.3)	0.001	0.008
Light physical activity time (min/day)	272.8 (247.4–298.2)	245.9 (221.0–279.9)	322.8 (289.0–356.6)	<0.001	0.032
Moderate to vigorous physical activity[a]					
Moderate to vigorous PA, % awake wear	0.1 (0.6)	0.1 (0.5)	0.4 (1.1)	0.266	n.s
Moderate to vigorous PA time (min/day)	2.0 (7.8)	1.4 (4.9)	3.4 (11.6)	0.292	n.s
Steps (number/day)	3677 (3083–4270)	2816 (2355–3278)	4941 (4109–5773)	<0.001	0.015
Meeting PA guidelines, n (%)[a]	7 (8.9)	3 (4.8)	8 (17.8)	0.054	n.s

All data (adjusted for age, body mass index and waking wear time) are presented as mean (95% CI) except for moderate-vigorous physical activity, which are presented as median (interquartile range)

*p value between baseline and 6 months after TKA (Bonferroni)

[a]p value calculated using generalized linear model; remaining data compared using linear mixed model

at 6 weeks compared to 6 months after TKA ($p = 0.013$) but was not different between baseline and 6 months after TKA.

Patients spent more of their awake wear time in LPA at 6 months after TKA compared to before ($p = 0.008$) and 6 weeks after ($p = 0.001$) TKA. Daily LPA time increased from baseline to 6 months after TKA by approximately 50.0 (95% CI 3.2–96.7) min/day ($p = 0.032$).

The patients spent less than 1% of their awake wear times in MVPA at all time points (Table 3). Approximately 5–18% of the patients met the current PA guidelines at baseline and after TKA. Patient step count was significantly lower at 6 weeks ($p < 0.001$) but significantly higher ($p = 0.015$) after surgery compared to baseline.

Patterns of accumulation of activity behaviors before and after TKA

Figure 2 shows comparisons of the accumulation of patients' awake wear times spent in sedentary, LPA and MVPA intensities accumulated for different bout lengths between baseline and 6 months after TKA. There were significant reductions in the percent of time spent in prolonged bouts of SB at 6 months after TKA compared to baseline. Bouts of varying durations of light activity also increased significantly between baseline and 6 months after TKA.

Figure 3 depicts the hourly variation of awake wear time not spent in MVPA (i.e., the sedentary to light activity ratios) over the course of the day. Overall patients were less

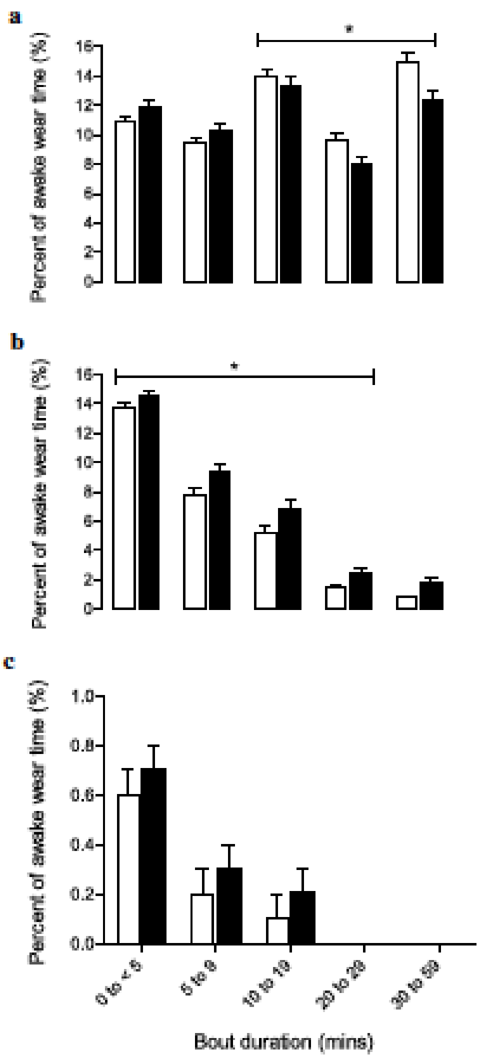

Fig. 2 Percentage of awake wear time spent in a sedentary behavior, b light physical activity and c moderate to vigorous physical activity before (white bars) and 6 months after (black bars) total knee arthroplasty. *$p < 0.05$ for indicated bouts between baseline and 6 months after TKA. Data are presented as mean (SEM)

sedentary in the early hours of the day (6h00–10h00), after which, time spent sedentary gradually increased through the afternoon to late evening (13h00–23h00). The sedentary to light ratio was similar between baseline and 6 weeks after TKA. However, between baseline and 6 months after TKA, there was a significant reduction in sedentariness and an increase in light activity from 09h00 to 19h00 ($p < 0.05$).

Discussion

The most important finding of this study is that overall total daily sedentary time and time spent in light physical activity improved 6 months after TKA with patients showing a reduction in SB of approximately 56 min and an increase in LPA of approximately 50 min per day. The patients also interrupted their sedentary time more frequently after TKA compared to baseline. In conjunction with the changes in objectively measured activity, the patient-reported activity and physical functional levels as well as physician-reported outcome (range of motion) significantly improved from baseline to 6 months after TKA, as was expected.

Although in the current study, the amount of time spent in SB at 6 months after TKA was higher than that of Brandes et al. [7] study (7.0 h/day, 56.5% of awake wear time), and lower than that reported in Harding et al. [18] study (11.6 h/day, 83% of awake wear time), to our knowledge a decrease in sedentary time of this magnitude has not yet been reported in TKA patients following their surgery. With no significant difference being observed in the time our patients spent in MVPA, it is likely that the time spent in prolonged SB decreased at 6 months after TKA, because it was interrupted more frequently with LPA.

Understanding the hourly patterns of SB and LPA provides a useful source of information for physician monitoring and for informing targeted interventions with the ultimate aim of improving overall health and quality of life [9]. The patients in this study accumulated similar volumes of SB and LPA in the early hours of the day (6h00–10h00) before and after TKA. However, there was a noticeable shift in total amounts of sedentary and light activity accumulated over the course of the day following TKA, but particularly at certain times of the day. There was less time spent in SB and more in LPA between 11h00–19h00 at 6 months after TKA compared to baseline. Light PA is associated with purposeful movements accumulated during performances of activities of daily living (ADL) [8]. The improvement in activity behaviors at a time of day when the patients were likely to be engaged in household, social and occupational activities, has implications for quality of life of patients in this study and may offer an explanation as to why such great improvements in activity behaviors were observed following TKA. Patients should be encouraged to engage in more light activity during these times, as the present study has shown that this is a feasible time for targeted interventions. This study supports the notion that targeted interventions may focus on improving activity behaviors of low intensities (SB and

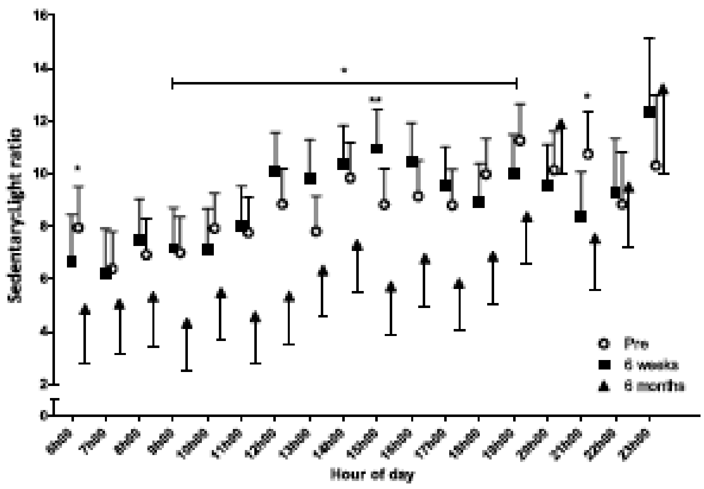

Fig. 3 Average hourly sedentary to light activity ratio between baseline and after TKA. Data are mean (95% CI) sedentary to light ratios per hour of the day for each of the three visits. Data are adjusted for awake wear time. *$p < 0.05$ between pre (filled circle) and 6 month post-TKA (filled triangle). **$p < 0.01$ between 6 weeks (filled square) and 6 month post-TKA (filled triangle)

LPA), even at 6 months postoperatively, where functional recovery appears to be optimal [2, 11, 36]. Long-term post-operative interventions aimed at offsetting sedentary time with LPA or task-oriented activities performed during ADLs may sustain recovery of functions, quality of life and physical activity in the long term.

The current study is the first to explore activity behaviors in a population living in a low to middle income country (South Africa) and this may also be a reason for the difference between this study and others who have reported no or marginal improvements in activity behaviors following TKA [2, 17]. The present study was conducted in patients of low socioeconomic status (with particularly, low educational background) compared to other studies done in high-income countries. Changes in daily routine and nature of work at home and workplace (due to urbanization and automatism of work and life) may result in a greater time spent being sedentary [16, 21]. Whereas individuals from high-income countries may be able to increase leisure-time PA in case of activity reduction due to work schedules [12], their counterparts in lower income groups (due to poor economic climates) tend to improve PA by performing activities of daily routines related to work, domestic chores and transport [3]. Furthermore, the drive or motivation to change activity behavior in patients with musculoskeletal disorders may vary from one socio-economic group to the other. Therefore, the inherent motivation to independently perform activities of daily living and return to work postoperatively may have resulted in improved activity behaviors of patients in the present. Herbolsheimer et al. [19] indeed showed that the impact of knee OA on activity behavior patterns varies from one socioeconomic group to the other [19]. In addition, methodological differences across studies may also explain the reason why the findings of the present study are different from the previous studies. The previous studies have either monitored activity of patients in less than 3 days [7, 15, 38, 39] and only a few between 4 and 7 days [18, 24].

The observation of a low accumulation of MVPA is consistent in all of the studies that have assessed PA in patients before and/or after TKA. In our study, less than 1.0% of the daily awake wear time was spent in MVPA at 6 months after TKA and less than a third of the patients met the PA guidelines at baseline and 6 months after TKA. Despite the high rate of success associated with TKA, a lower recovery rate compared to THA, post-surgical pain and quadriceps muscle weakness have all been found to mitigate physical functioning [5, 11, 28, 31]. All of the patients in this study had advanced knee OA prior to surgery and they may have had underlying musculoskeletal damage as a consequence of the knee OA that inhibited more intense movements. Patients were also on average 65 years of age and most older adults do not achieve the recommended PA guidelines even in the absence of a musculoskeletal disorder [35]. However, in this study, the number of steps per day of the patients both at baseline and 6 month post-surgery is consistent with the reported values for healthy 65–69-year adults in the National Health and Nutrition Examination Survey (NHANES) (3302–5269 steps/day) [37]. The patients in this study may, therefore, have already been relatively lightly active and may have been further motivated to increase their activity post-surgery in the lower intensity activities. A longer duration of recovery may allow such patients to adopt a more moderately intensively active lifestyle [15].

There are a few limitations associated with this study. There was high rate of dropout at follow-up, which decreased the total number of patients completing the 6-month follow-up. However, the characteristics of these patients were similar to those included in the analysis. Furthermore, we intended on recruiting 107 patients, but found a significant reduction in SB after preliminary analysis and, therefore, believe that the study was adequately powered. The use of accelerometers comes with the challenge of different algorithms and decision rules for cut points for PA and SB. This makes comparison with other studies limiting; for instance, the ActiGraph GT3X has not been used in patients undergoing TKA in a longitudinal study design before. In addition, waist-worn accelerometers do not always adequately measure activities including upper body activities or upright activity behaviors of low ambulatory components such as cycling [26]. However, in the present study no patient-reported cycling in the UCLA activity index during the activity monitoring periods. Importantly, the same intensity measured by an accelerometer will in reality translate to a different level of cardiorespiratory impact on different people. Thus, it is important to have accelerometer cut point algorithms validated for specific populations (for example, in those with musculoskeletal disorders) [30].

Conclusion

In line with an improvement in patient-reported pain, stiffness and physical function 6 months after total knee arthroplasty, overall objectively measured light physical activity increased and sedentary behavior decreased 6 months after total knee arthroplasty. The way that patients accumulated their activity throughout the day also improved after surgery with patients spending more time in light activity during the active hours of the day. Clinically, functional improvement in patients following total knee arthroplasty may be assessed by objectively measuring changes in low intensity activity behaviors. This comprehensive analysis of detailed daily activity behaviors can be used to inform feasible interventions for increasing the duration of light physical activity bouts and decreasing prolonged sedentary bouts to improve quality of life and overall health following TKA.

Author contributions EF participated in conceptualization of study, development of study design, collecting data, writing of drafts, editing of drafts. JAM participated in conceptualization of study, development of study design, writing of drafts, editing of drafts. DVDJ took part in conceptualization of study, development of study design, editing of drafts. LM took part in conceptualization of study, development of study design, editing of drafts. YSK took part in development of study design, collecting data, editing of drafts. MT took part in conceptualization of study, development of study design, editing of drafts. RMM participated in conceptualization of study, development of study design, writing of drafts, editing of drafts. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest LM wishes to declare that he has offered consultancy services for Implantcast for the development of a new prosthesis. No money has been paid for these consultancy services. The remaining authors declare that they have no conflict of interests.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (clearance certificate number M150323) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent An informed consent was obtained from all individuals participants included in the study.

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