The Effectiveness of a Lateral Wedge Insole on Knee Pain, Physical Activity and Joint Loading in Individuals with Medial Knee Osteoarthritis

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List of abbreviations

A	*Anterior*
AAOS	*American Academy of Orthopaedic Surgeons*
ACR	*American Collage Rheumatology Criteria*
ADL	*Activity of Daily Living*
ALF	*Aggregated Locomotor Function score*
AL	*Anterior-Lateral*
AM	*Anterior-Medial*
ANOVA	*Analysis Of Variance*
ASIS	*Anterior Superior Iliac Spine*
BMI	*Body Mass Index*
CAST	*Calibrated Anatomical System Technique*
CKL	*Cumulative Knee Loading*
CMC	*Coefficient of Multiple Correlation*
COM	*Centre Of Mass*
COP	*Centre Of Pressure*
DOF	*Degree of Freedom*
3D	*3-Dimensional*
EULAR	*European League Against Rheumatism*
EKAM	*External Knee Adduction Moment*
HRQoL	*Health-Related Quality of Life*
GRF	*Ground Reaction Force*
HOT	*High Tibial Osteotomy*
HAP	*Human Activity Profile*
ICC	*Intra-class Correlation Coefficient*
ICOP	*Intermittent and Constant Osteoarthritis Pain*
IDEEA	*Intelligent Device for Energy Expenditure and Physical Activity*
KAAI	*Knee Adduction Angular Impulse*
K/L	*Kellgren and Lawrence*
KOOS	*Knee Injury and Osteoarthritis Outcome Score*
L	*Lateral*

LWI	*Lateral Wedged Insole*
M	*Medial*
MCS	*Mental Component Scale*
MMD	*Minimal Detectable Difference*
MRI	*Magnetic Resonance Imaging*
N	*Neutral*
NHS	*National Health Services*
NICE	*National Institute of Health and Clinical Excellence*
NSAID	*Non-Steroidal Anti-Inflammatory Drugs*
OA	*Osteoarthritis*
P	*Posterior*
PA	*Physical Activity*
PASE	*Physical Activity Score for the Elderly*
PCS	*Physical Component Scale*
PIS	*Participant Information Sheet*
PL	*Posterior-Lateral*
PM	*Posterior-Medial*
POSE	*Position and Orientation of the body segments*
PSIS	*Posterior superior Iliac Spine*
QoL	*Quality of Life*
QTM	*Qualisys Track Manager*
RCT	*Randomised Controlled Trials*
REP	*Research Ethics Panel*
ROM	*Range of Motion*
SD	*Standard Deviation*
SEBT	*Star Excursion Balance Test*
SEM	*Standard Error of Measurement*
SF-12	*12-Items Short-Form Health Survey*
SPSS	*Statistical Package for the Social Sciences*
ST	*Step Test*
TKR	*Total Knee Replacement*
UKR	*Uni-compartmental Knee Replacement*
VAS	*Visual Analogue*

VM	*Vastus Medialis*
V3D	*Visual 3-Dimensional*
WHO	*World Health Organization*
WOMAC	*Western Ontario and McMaster Universities Arthritis Index*

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Abstract

Knee osteoarthritis (OA) is the most common chronic musculoskeletal diseases causing knee pain, disability and reduced levels of activity. Medial compartment of the knee joint is commonly affected, nearly 10 times more frequently, than lateral compartment by the disease. Knee loading (i.e. External Knee Adduction Moment (EKAM)) is higher in individuals with medial knee OA compared with healthy subjects. Lateral wedge insoles (LWI) are designed to reduce the knee loading by altering the Ground Reaction Force (GRF) vector more laterally to be closer to the centre of the knee joint (still acting medially to the knee joint) and thereby reduces the moment arm to reduce EKAM and an improved clinical outcome. The aim of this study was to determine the effect of LWI on knee pain, level of physical of activity and EKAM in during walking. To accomplish the research, firstly, a reproducibility trial was conducted with individuals with medial knee OA to investigate the consistency of the instrument in producing the same results at different time points. In addition, to ensure that the differences between measurements at the end of the intervention are the effect of the intervention itself. Secondly, the main study was performed to identify any change or improvement in knee pain, level of activity and knee loading in twenty participants with medial knee OA after wearing LWI compared to baseline and comparator group during walking. Data were collected at three time-points; baseline, week one, and week six where an activPAL3 monitor was placed on participant's thigh for 7 consecutive days to measure their activity level each time. There was no difference between the groups in the characteristics and primary outcomes at baseline. The results of this study have demonstrated a further understanding of LWI effectiveness where the group wearing LWIs demonstrated a reduction in EKAM and pain with improvement in physical activity. Individuals walked more, faster and for a longer time when wearing LWI for six weeks. Therefore, activity profiles of individuals during interventions give important information and it has been recommended to collect to complete the profile of the individuals. Future larger studies to find out the biomechanical, clinical (pain and level of activity) and radiological changes after wearing LWI is needed to determine whether progression of knee OA can be delayed.

Chapter One

INTRODUCTION

Osteoarthritis (OA) is a common musculoskeletal disease mainly affecting the knee joint, causing disability, particularly in the elderly (Woolf and Pfleger, 2003). The prevalence of the disease increases with age, especially those into their fourth decade of life (Jordan et al., 2007), and women are the most frequently affected (Srikanth, 2005). In the UK, roughly 8.5 million people have osteoarthritis (4.7 million have knee OA) and it is expected to increase to 17 million by 2030, which is estimated to cost 1% of the annual Gross National Product (Arthritis Care, 2012; Arthritis Research, 2015). Thus, knee OA is costly and has a significant effect on the society. It not only causes disability, but also is responsible for a high number of lost working days and a high rate of spending for medical health services (Kotlarz et al., 2009; Bitton, 2009).

Knee pain, joint swelling, decreased knee joint range of motion, crepitus in the joint, and morning stiffness are the common symptoms in knee OA (Bijsma and Knahr, 2007). There are two kinds of risk factors which could increase the occurrence of knee OA and accelerate the progression of the disease. Firstly, systemic risk factors such as age, gender, bone density, and genetic predisposition. Secondly, local biomechanical risk factors affect such as obesity, muscle weakness, amount of knee loading, previous joint injury and deformity (Felson et al, 2000). The latter are the potential modifiable ones and where research in osteoarthritis is focussed.

In knee OA, the medial tibiofemoral compartment is ten times more frequently affected than the lateral tibiofemoral compartment (Ahlback, 1968) primarily because it is exposed to 2.5 times greater load than the lateral compartment during gait, and the line of the ground reaction force (GRF) passes medially to the medial compartment of the knee joint (Schipplein and Andriacchi, 1991). Therefore, the load increases on the knee joint across the medial compartment, as indicated by the External Knee Adduction Moment (EKAM), which is a surrogate measure of medial knee load during ambulation (Schipplein and Andriacchi, 1991, Hinman et al., 2013). In addition, individuals with knee OA have been shown to have a higher EKAM compared to healthy subjects (Schipplein and Andriacchi, 1991; Huang et al., 2008; Mündermann et al., 2005). A higher EKAM during walking is a very strong predictor of the presence of the disease (Baliunas et al., 2002), disease severity (Huang et al., 2008; Mündermann et al., 2005), and develop osteoarthritis progression

(Miyazaki et al., 2002, Chang et al., 2015) as varus knee alignment is the best predictor of a high EKAM (Barrios et al., 2009a; Chang et al., 2015).

In addition, the risk of presence and progression of medial knee OA is associated with higher loading on the medial compartment of knee joint (Miyazaki et al., 2002, Bennell et al., 2011b, Chang et al., 2015) and disease severity is increased with a higher EKAM (Sharma et al., 1998; Miyazaki et al., 2002; Hurwitz et al., 2002; Thorp et al., 2006; Landry et al., 2007; Huang et al., 2008). Sharma et al (1998) demonstrated that the magnitude of the EKAM associated with severity of medial tibiofemoral OA. The risk of disease progression of medial knee OA increased 6.46 times when the magnitude of the EKAM increased by 1% and a higher peak EKAM has been shown to predict and be associated with OA progression in patients with medial compartment knee OA (Miyazaki et al., 2002). Evidence has shown that mechanical loads play a vital role in the development and progression of medial knee OA. In medial knee OA, a higher EKAM will cause excessive loading on the medial tibiofemoral knee joint during stance phase and thereby accelerate the disease progression over the time. The peak of the EKAM in individuals with medial knee OA was correlated with higher pain level and the study suggested that reduction of medial knee loading may lead to pain relief (Maly et al., 2008; Hinman et al., 2008). Therefore, reduction of the EKAM should be a target for management of the condition to reduce knee loading and knee pain.

Coincidentally, the restriction of physical activity appears in 80% of individuals with knee OA and 25% cannot perform their major daily activities (WHO, 2003). The reduction in activity level is mainly due to increased knee pain and the fear of falling during the physical activity (McAlindon et al., 1992; Fitzgerald et al., 2004). Reducing the level of activity is also associated with the majority of health problems such as obesity, heart disease, diabetes, and hypertension (Pedersen et al., 2006). Moreover, a reduction in the activity level (i.e. number of steps), an inactive behaviour and sedentary time (spent more time in sitting and lying position) increases in individuals with knee OA are the main characteristics of patients with knee OA (Dunlop et al., 2011). Dunlop et al., (2014) demonstrated that sedentary behaviour by spent more time in sitting and inactive has a significant relationship with knee OA and considered this as a significant risk factor in individuals with knee OA and cause disability over two years. Duvivier et al., (2013) found that reducing inactivity behaviour by increasing stepping time and standing time is more effective in type 2 diabetes than one hour of physical exercise. Moreover, improving the physical activity by increasing the number of steps has been recommended for individuals with knee OA (Wallis et al., 2013). However, studies have shown that individuals who stepped more than 10,000 steps/day were associated with a greater

risk of cartilage damage by 1.52 times in elder individuals (Dore et al., 2013), increase the risk of progression of knee OA (Lin et al., 2013). Similar result (1.35 times) was found by Kumar et al (2014) who assessed 160 subjects with knee OA over one year. Moderate physical activity (7,500-9,999 steps/day) was recommended with knee OA (Dore et al., 2013; Lin et al., 2013; Kumar et al., 2014; White et al., 2014) to reduce the risk of cartilage damage. Therefore, the emphasis of treatment should be to reduce load on the knee joint, relieve knee pain to increase the overall activity. This can be achieved by using suitable approaches of treatment with appropriate physical activity instruments to measure the effectiveness of the intervention (Karapolat et al., 2009).

Knee osteoarthritis is responsible for reduced physical function (White et al., 2014) increased pain, reduced muscle strength and joint space narrowing, and thereby a reduced activity level (White et al., 2013). Although there is no known cure (Waller et al., 2013), a variety of treatment approaches attempt to reduce the load on the knee joint, limit the symptoms of knee osteoarthritis and potentially delay disease progression. To achieve these goals of treatment, there are various methods such as surgical interventions, pharmacological, and non-pharmacological approaches.

Surgical intervention aims to reduce the load on the affected knee joint when non-surgical intervention fails to reduce the load or decrease the symptoms (Wada et al, 1998). However, whilst surgical intervention (total knee replacement) has a good to excellent results, some functional limitations are still there and some patients may not suitable or may not want for this surgery (Callahan et al., 1994). In addition, High Tibial Osteotomy (HTO) and Unicompartmental Knee Replacement (UKR) have been recommended for younger patients to re-distribute the load from the medial compartment of the knee joint for HTO, and to maintain the normal knee function for UKR; however, the loading on knee joint tends to increase gradually over one to five years after HTO and leading to a total knee replacement over the time (Grelsamer, 1995).

Lane et al., (2010) found that tanezumab drug (common uses to reduce knee pain in osteoarthritis) reduced knee pain during walking by 45-62% from baseline; however, individuals with knee OA were going for a knee replacement too early (Lane et al., 2010). Therefore, whilst analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) have a significant effect on pain in individuals with knee OA, EKAM is increased and thereby disease progression was found to be developed over time (Schnitzer et al., 1993; Huskinsson et al., 1995). Therapeutic exercises are considered as a core treatment for individuals with medial knee OA and are the primary approach for the management of knee OA demonstrating reduced knee pain and improvements in knee function (Zhang et al., 2008; NICE, 2008; Hung et al., 2003). However, recent research has shown that exercises do not reduce

the load on the knee joint in knee OA (Bennell et al., 2010; Al-Khlaifat et al., 2015). Therefore, pain reduction with a high EKAM may accelerate disease progression over time (Andriacchi, 1994).

Lateral-wedge insoles (LWI) and valgus knee braces are considered as conservative management techniques where they decrease loading on medial compartment of knee joint, improve pain and function in individuals with medial knee OA. In a crossover randomised study by Jones et al (2013a) who investigated the effect of LWI and valgus knee brace on knee pain, function, and knee loading in individuals with medial knee OA. Jones et al (2013a) concluded that the both treatments reduced the EKAM and Knee Angular Adduction Impulse (KAAI); however, the insoles were more acceptable by the patients compared to valgus knee brace. The KAAI considers a magnitudes and duration of the load on the knee joint (Thorpe et al., 2007). Lateral-wedge insoles are considered as a conservative intervention in individuals with knee osteoarthritis to reduce the EKAM and KAAI (Barrios et al., 2013; Hinman et al., 2009 & 2013). They are a low-cost intervention, simple to use, and were first reported by Sasaki and Yasuda in 1986 (Sasaki and Yasuda in 1986). Lateral-wedge insoles have been shown to be an important intervention to reduce the EKAM by shifting the ground reaction force laterally by altering the angle of the calcaneus into a valgus position (Pollo et al., 1998), and thereby decreasing the moment arm which results in a reduced the EKAM on the knee joint (Kakihana et al., 2005; Jones et al., 2014), and thereby potentially reducing the progression of knee OA (Miyazaki et al., 2002). Evidence has found that the EKAM was reduced significantly by wearing LWI (Barrios et al., 2013) but pain and function did not improve compared to neutral insoles (Pham et al., 2004; Baker et al., 2007; Bennell et al., 2011b; Parkers et al., 2013). One potential reason is that the individuals received a placebo effect from the neutral insoles and thereby no significant differences were seen between LWI and neutral insoles in term of knee pain reduction. In addition, while pain level is of utmost importance, the overall activity level of the individual may have changed with LWI and the individual may have walked to their respective pain level. Therefore, it is not known if there is a change in the activity level of the individual when using with lateral wedge insoles which may counteract the reduction in symptoms that the individual is experiencing when on treatment. Moreover, improvements in physical activity level should also be targeted with any treatment (Holsgaard-Larsen and Roos, 2012) especially from the health relating living aspect. If a treatment that has no biomechanical effect (e.g., neutral insole) but has a placebo pain relief, activity improvement may be expected to see which cumulatively would increase the loading on the medial compartment of the knee. Conversely, if the treatment has a biomechanical effect (e.g., lateral wedge insole), with pain reduction and improvement of activity, a potential cumulative reduction in loading on the medial compartment would be seen. In addition, the

cumulative loading may be increased over time with LWI if the reduction was not large enough as reduction not be as much as higher EKAM with neutral insoles and reduced level of activity. However, to our knowledge, this is not known in the current literature.

There are numerous questionnaires that give indications of activity level but they are unreliable (Washburn and Montoya, 1986). Therefore, monitors that constantly record activity are recommended to measure the level of activity objectively. One of these monitors is the activPAL3 (PAL Technologies, UK) which measures the amount of time spent sitting, lying, standing, stepping, and cadence (Dahlgren et al., 2010). This monitor has been validated to measure static and dynamic activity in adults (Godfrey et al., 2007). The activPAL3 is more valid to measure sedentary behaviour of the older population compared to Actigraph (Lyen et al., 2012) and it is better and more valid to measure slow walking than the Actigraph and pedometer. In addition, there has been shown to be a strong correlation between activPAL3 and video observation in measuring time spent in different position and number of steps in different speeds (Granat et al., 2007). The activPAL3 monitor is also more sensitive to any reduction in sitting time compared to other monitor (Actigraph) and it is recommended to measure sedentary time in inactive, overweight, and older adults (Kozey-Keadle et al, 2011; Lyden et al., 2012). Therefore, using the activPAL3 is a novel instrument to measure the level of activity of individuals with knee OA.

In summary, evidence has shown that the external knee adduction moment is reduced significantly when using lateral-wedge insoles, however, pain and physical function do not improve significantly (Baker et al., 2007; Bennell et al., 2011b; Radzimski et al., 2012; Parkes et al., 2013). However, it is not known if a change in the activity level of the individual is seen with lateral wedges which may counteract the reduction in symptoms that the individual is experiencing when on treatment.
No study has investigated the effect of lateral-wedge insoles on activity level using an activity monitor. The primary aim of this study is to determine whether a lateral wedged insole improves the level of physical activity in individuals with medial knee OA, when compared to neutral insoles.
Potentially, the lateral wedged insoles could decrease the load on medial compartment of knee joint and reduce knee pain and thereby improve physical activity in individuals with medial knee OA.
Therefore, the importance of the study can be highlighted in the following; the results of this study will help us to further understand the clinical and biomechanical effect of LWI as efficient treatments for early stage of medial knee OA. It has been proposed that walking with pain does not increase the progression of knee OA if the EKAM reduced when using lateral wedged insoles. In addition, the reduction in the EKAM will lead to improvement in the level of physical activity.

In the next chapter, a review of the literature related to knee OA, knee loading, level of physical activity in knee OA, and management are presented to demonstrate the gaps from the previous studies.

To ensure the results of our study are accurate, a test-retest reliability study is presented in chapter three to test the reliability of the outcomes measures which will be investigated in the main study. The reproducibility study is undertaken to ensure the differences between outcomes at pre-intervention and post-intervention are the results of the intervention itself and not of measurement error or investigators` error in measuring the outcomes.

The effectiveness of the lateral wedged insoles on knee pain, level of physical activity, and knee loading in individuals with medial knee OA will be investigated in chapter four with an overall conclusion and future studies in chapter five.

Chapter Two

LITERATURE REVIEW

2.1. Definition of osteoarthritis

Osteoarthritis (OA), also known as degenerative joint disease, is one of the most common chronic musculoskeletal diseases causing pain, loss of function, decreased level of activity, and disability (Woolf and Pfleger, 2003). OA is also defined as a slow progressive degenerative disease affecting articular cartilage of the joints and subchondral bone (Sangha, 2000). According to the European League Against Rheumatism (EULAR) (2015), pathological changes seen on X-ray or the presence of disease signs or both can be considered part of the definition of OA disorder, and therefore X-ray findings and the presence of joint pain on the most days are preferred detection methods. Therefore, OA is defined as a heterogeneous group of conditions that lead to joint symptoms and signs associated with damage of articular cartilage (Altman et al., 1986).

Clinical symptoms and signs that occur with OA are joint pain, inflammation, morning stiffness (< 30 minutes), swelling, crepitus with movement, limitation of movement and instability (Buckwalter et al., 2004; Sharma et al., 2006). Additionally, OA is characterised by progressive loss of articular cartilage and new bone formations at the joint margins (osteophytes) (Altman et al., 1986; Sangha, 2000). Although, hip, knee, and hand joints are common sites for OA (Hunter and Felson, 2006), the knee joint is two times more frequently affected than hip and hand joints (Oliveria et al., 1995) because the knee joint is one of the body`s primary weight-bearing joint (Slemenda, 1992; Felson et al., 2000).

2.2. Knee osteoarthritis

Knee OA is a degenerative disorder resulting in articular cartilage damage, bone changes, and inflammation of a synovial membrane (Mankin et al., 1981; Benito et al., 2005; Jacobson et al., 2008) (Figure 2-1). Knee osteoarthritis starts in the areas which are not designed to undergo excessive and repetitive loading (Mankin et al., 1981). Thickening of subchondral bone appears with knee OA, leading to formation of osteophytes (Burr, 2003). In addition, the joint surface is covered by a thin layer of collagen matrix, which is important for the cartilage to protect the knee joint from

friction and to distribute the load. As a result of the excessive and repetitive loading this layer is destroyed and cartilage degrades with the disease (Dijkgraaf et al., 1995). Moreover, inflammation of the synovial membrane occurs in knee OA as a result of repetitive stress (Benito et al., 2005).

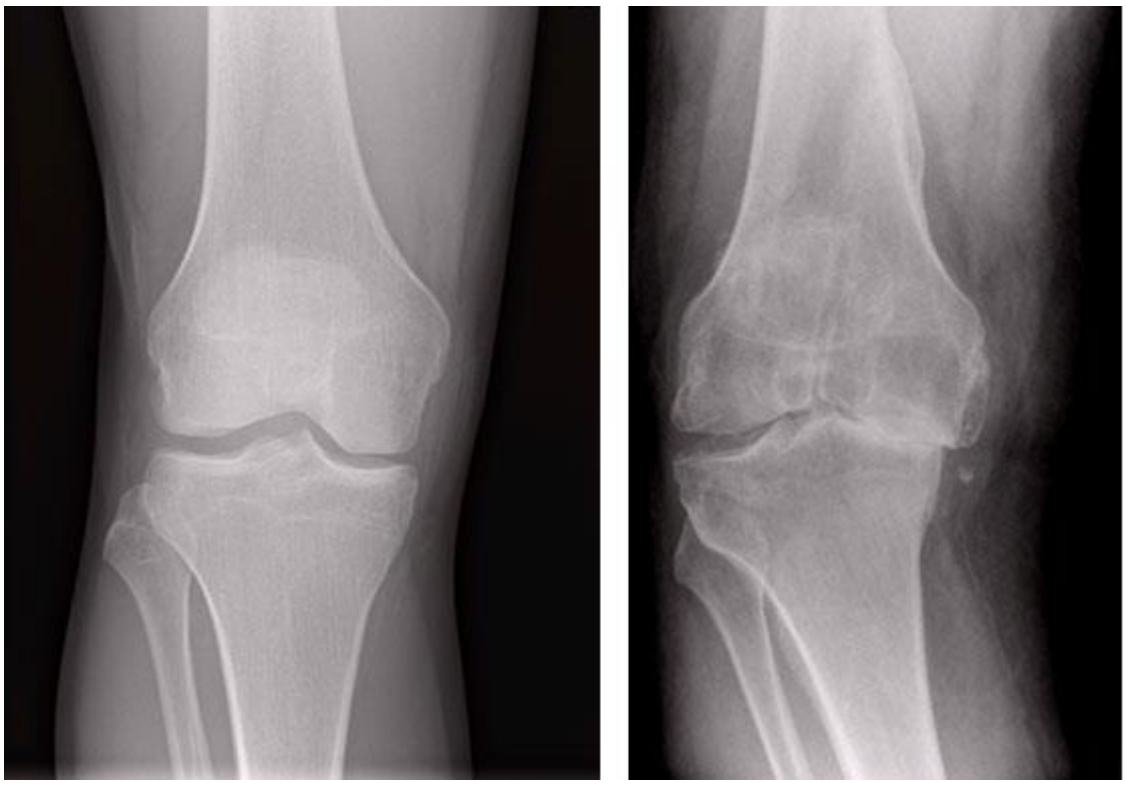
A  **B**

Figure 2-1: (A) Normal Rt) knee, (B) Changes in the Rt) knee result in osteoarthritis (kneesurgeon.com.au)

Knee OA is associated with pain, functional disability, morning joint stiffness, crepitus, and a low level of activity (Jordan et al., 2003; Keysor, 2003). Although, knee pain is considered as a primary sign in patients with knee OA (Lohmander et al., 2004), the source and causes of pain are complex and not well understood (Hunter et al., 2008). However, knee pain is potentially caused by the increased repetitive stress and the amount of load on knee joint, there are other factors that may contribute to pain, for example laxity of the ligaments, joint capsule or subchondral bone (Dieppe and Lohmander, 2005; Jones et al., 2014). Gooberman-Hill et al., (2007) found that individuals with knee OA experienced intermittent knee pain and it varied according to activity and day by day. Muscle weakness was reported in individuals with knee OA (Slemenda et al., 1997) in addition to laxity of the knee ligaments (Felson et al., 2000), and therefore knee joint instability and function limitations occur in patients with knee OA (Hurley et al., 1997).

Additional possible symptoms have been reported in individuals with knee OA, such as joint deformity, psychological stress, and altered gait (Hunter et al., 2008). Limitations in performing essential daily activities, such as mobility outside the home and work duties, appeared in 8,000 out 10,000 patients with knee OA in a study by Fautrel et al., (2005).

2.3. Incidence and prevalence of knee OA

There are approximately 8.5 million people in the UK diagnosed with osteoarthritis and the number is expected to increase to 17 million by 2030 (Arthritis Care, 2012). In addition, OA prevalence increases with age, especially in the fourth decade of life (Jordan et al., 2007). Radiographic OA (changing in joint structure) increases in older people and over 80% of those are over the age of 75 (Kellgren and Lawrence, 1975). In the Framingham study, the prevalence of knee OA was 30% in individuals aged 64 years or older (Felson et al., 1987) and one in ten individuals over the age of 60 in the United States has knee OA (Zhang and Jordan, 2010). The prevalence of knee pain increases with age (Grotle et al., 2008) and radiologic knee OA increases as a result of knee pain in individuals who are over the age of 55 (Peat et al., 2001). However, the correlation between knee pain and the radiographic features of knee OA is not constant (Arden and Nevitt, 2006).

The prevalence and incidence of knee OA have been found to be higher in women than men (Felson et al., 2000), and women are two-times more likely than men to have knee OA (Davis et al., 1991a), this could be explained by the postmenopausal estrogen deficiency (Felson et al., 1997). It estimated that OA affects 18% of women over 60 years-old compared to 9.6% of men at the same age group (WHO, 2003). Oliveria et al., (1995) found that the incidence of symptomatic knee OA increases by 1% per year in women over 50 years of age. In a Norwegian population aged between 24 and 76 years, the prevalence of knee OA was 6.2% in men and 7.9% in women (Grotle et al., 2008). This may be explained by the higher prevalence of obesity in women compared to men and men had stronger muscles compared women (Davis et al., 1998; Felson et al., 2002).

In Germany, 86% of women and 77% of men visited their general practitioner suffering from knee pain and diagnosed with osteoarthritis inside their knee (Rosemann et al., 2007). In Korea, knee OA affects 53.8% of women and 17.1% of men and bilateral knee OA is more common than unilateral knee OA (Cho et al., 2011). OA appears to be more frequent among women than among men (Arden and Nevitt, 2006), this could be due to sport participation (Felson et al., 2002).

Jordan et al (2004) found that 18.1% of individuals who visited their general practitioner had symptomatic knee OA, and the prevalence of symptomatic OA of the knee was 4.4% compared to 0.7% and 2.5% for hip and hand, respectively (Arden and Nevitt, 2006).

2.4. Economic cost of knee osteoarthritis

The annual cost of healthcare for osteoarthritis patients was approximately 2.15 times the non-osteoarthritis patients (Maclean et al., 1997). In Canada, the cost of osteoarthritis was estimated at $5.9 billion in 1994 or approximately $700 per patient per year (Coyte et al., 1998). A new study was done in Canada by Gupta et al. (2005) which estimated the cost of osteoarthritis by approximately $3000 per person. Lapsley et al. (2001) stated that the annual direct costs to the individual were average $258 and $537 per person in Australian. An approximately 8.5 million of the UK population have OA, which is estimated to cost 1% of the annual Gross National Product (NICE, 2008). Therefore, the cost of knee OA and it is treatment are very important consideration for patients, physiotherapists, clinicians, health care providers when making decisions about the management of knee OA (Losina et al., 2015). The high economic cost of osteoarthritis is a result of both direct and indirect costs. Direct costs represent day hospital, routine visits, drugs, physiotherapy, and transport, and temporary caregiver where hospitalization and physiotherapy were higher cost. Indirect costs represent working days lost and loss of productivity (Leardini et al., 2004). Individuals with knee OA experienced at last one of the following; work limitations, loss of workdays, need caregiver, decreased working hours, inability to find suitable employment and early retirement (Pincus et al., 1989; Leardini et al., 2004). In the UK, a recent report found that 36 million working days are lost due to OA, which is estimated to cost £3.2 billion (Arthritis Care, 2012). The lost productivity at work and home due to disability (OA) was estimated to cost $ 3.7 billion (Coyte et al., 1998). Gabriel et al., (1997) reported that the average costs for home care, childcare and reduce productivity were $281 in the USA.

In view of the high costs associated with knee OA and the prevalence of OA developing, it is important to understand the natural cause of knee OA in order to find preventative and effective therapies, decrease the direct and indirect cost, and reduce risk factors for both the incidence and progression of knee OA.

2.5. Diagnosis of knee osteoarthritis

Knee OA is characterised by knee pain, morning stiffness, tenderness, bone enlargement, crepitus, articular cartilage degradation, and joint space narrowing (Altman et al., 1986; Kevin et al., 2012). Therefore, knee OA is diagnosed either subjectively, depending on signs and symptoms such as knee pain, morning stiffness (< 30 minutes), age (> 40 years-old), crepitus, and bone enlargement (Dieppe and Lohmander, 2005), or objectively, depending on X-ray findings such as erosion of the articular cartilage, bone changes (presence of osteophytes), sclerosis, and joint space narrowing (Altman et al, 1986).

The American College of Rheumatology (ACR) clinical criteria for the classification of knee OA are a common and valid method which is used widely in studies and clinics to diagnose symptomatic knee OA. These criteria depend on the knee pain and the presence of osteophytes (formation of the bone at joint margins) associated with morning stiffness (<30 minutes) or patient's age (>50 years) or crepitus in the joint (Altman, 1987).

From a radiological perspective, the Kellgren and Lawrence scale (K/L) is used to quantify the severity of the disease using X-rays (Kellgren and Lawrence, 1975). This scale is used to assess radiographic knee OA and is divided into five grades: 0 = normal; 1 = possible osteophytes (doubtful OA); 2 = definite osteophytes, possible joint space narrowing (mild OA); 3 = moderate osteophytes, definite narrowing, some sclerosis, possible attrition (moderate OA); and 4 = large osteophytes, marked narrowing, severe sclerosis, define attrition (severe OA) (Kellgren and Lawrence, 1975; Chang et al., 2005) (Figure 2-2).

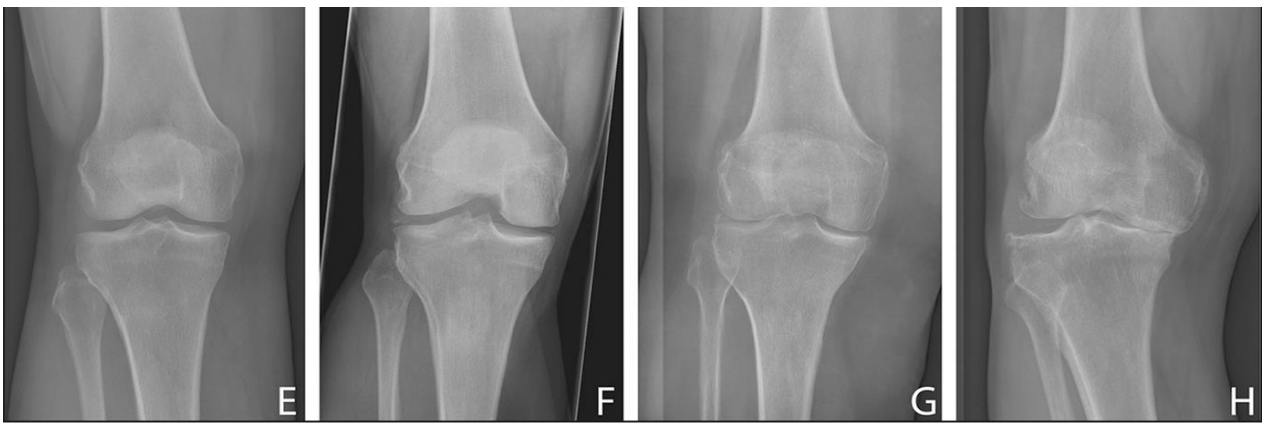


Figure 2-2: The Kellgren and Lawrence to measure severity of the disease (Radiographic Knee OA); E = KL grade 1, F = KL grade 2, G = KL grade 3, H = KL grade 4. (Kellgren and Lawrence, 1975)

Presence of knee pain is associated with knee OA and it is important for the clinical diagnosis (Neogi et al., 2009; Zhang et al., 2011; Guermazi et al., 2012). Moreover, the range of movement of the joint is often restricted, and there is generally pain with movement (Felson, 2006) in addition to activities such as climbing stairs, getting out of a chair, and walking long distances which bring on pain (Altman et al., 1986). Quadriceps weakness, knee joint instability, and functional limitation were noticed in individuals with knee OA (Hurley et al., 1997, Felson et al., 1997). Knee OA can be diagnosed in relation to affected side of the knee joint; medial tibiofemoral compartment, lateral tibiofemoral compartment, and patellofemoral joint. The medial tibiofemoral compartment is ten times more frequently affected by OA than the lateral tibiofemoral compartment by OA (Ahlback, 1968) (explained in section 2.9). The initiation and progression of knee OA have been proposed to be due to certain risk factors.

2.6. Risk Factors

Knee OA is a progressive degenerative disease with multiple risk factors. There are several risk factors affect the occurrence of knee osteoarthritis and the risk of disease progression (Fitzgerald and Oatis, 2004). Risk factors can be classified in two categories; systemic factors and local biomechanical factors (Felson et al., 2000) (Figure 2-3)

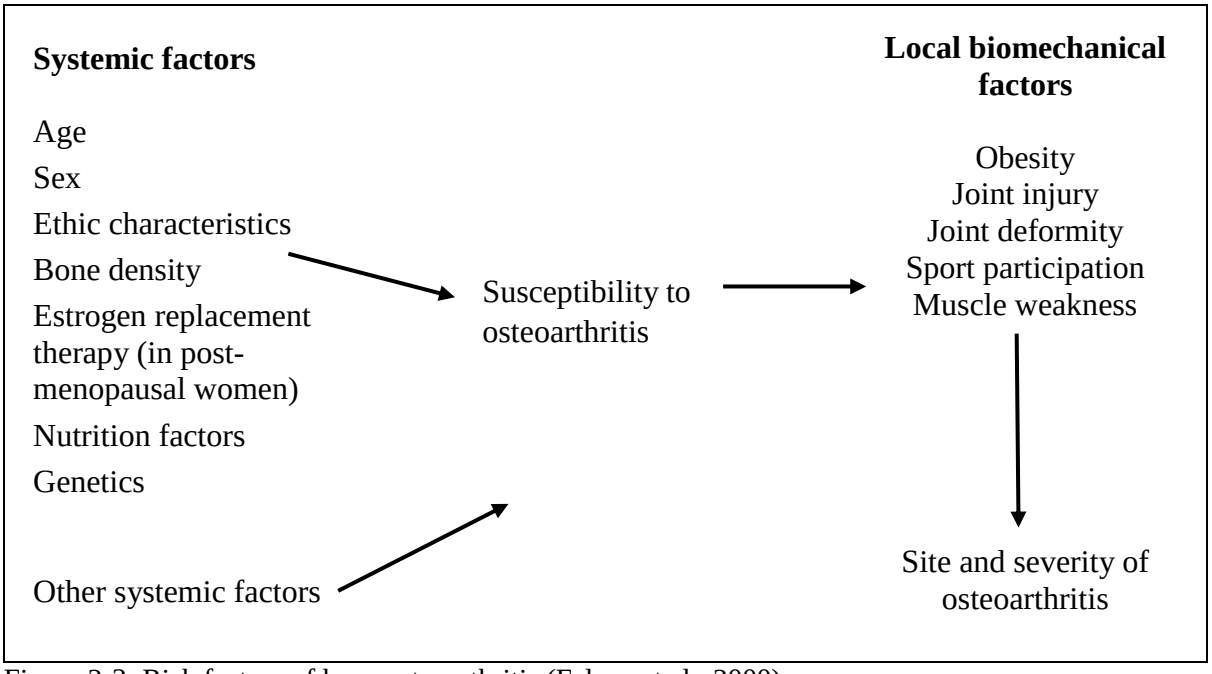


Figure 2-3: Risk factors of knee osteoarthritis (Felson et al., 2000)

The systemic and local biomechanical factors will be explored briefly below:

2.6.1. Systemic factors

a) Age: The prevalence of knee osteoarthritis increases with age (Peat et al., 2001). Osteophytes, cartilage lesion, and joint space narrowing are common in older people (> 50 years-old) (Guermazi et al., 2012). Additionally, the ability to protect cartilage is deceased with age (Payne et al., 2010).

b) Sex: In general, knee OA is more common in women compared to men (Wright, 2008) and uncommon in both gender under 40 years (Silman and Hochberg, 2001). Men under 50 years have a higher prevalence and incidence of knee OA compared to women. Whereas, women over 50 years have a higher prevalence (Felson et al., 1997; Silman and Hochberg, 2001). Women have a greater prevalence of medial joint space narrowing and a higher varus alignment than men (Wise et al., 2012; Kumar et al., 2015). In addition, women are more commonly affected by osteoarthritis than men due to the role of postmenopausal estrogen deficiency increasing the risk of OA and consequence of several biologic changes (Felson et al., 1995 & 1997).

c) Ethnic characteristics: Ethnicity has also been shown to be a risk factor for knee osteoarthritis in African-American patients than in white people (Jordan et al., 1996). In addition, a higher percentage of Chinese women complain of knee osteoarthritis in comparison with white women (Zhang et al., 2001).

d) Genetics: Genes are a strong risk factor for OA; however, not all joints have the same genetic susceptibility (Spector and MacGregor, 2004). Genetics increases the risk of incidence of knee OA after injury (Loughlin, 2003).

e) Oestrogen effect: A reduction in level of oestrogen hormone in post-menopausal women may be accompanied by an increase in the prevalence and incidence of knee OA. Coincidentally, there is greater risk of knee OA in pre-menopausal women as the hormone raises bone mass, increasing the load on the knee cartilage (Nevitt and Felson, 1997; Richette et al., 2003).

f) Antioxidants: The risk of incidence of knee OA may be increased by a reduction in vitamins C and D. Older individuals with low dietary intakes of vitamin C have greater progression of knee OA and associated with knee pain (McAlindon et al., 1996). There is

also an increased risk of incidence and progression of knee OA with low levels of vitamin D in older women (Parfitt et al., 1982; Raczkiewicz et al., 2015).

g) Bone density: Bone density has an important role in the initiation and progression of knee OA. High bone density increases the risk of knee OA and it is strongly associated with presence of osteophytes (MacGregor et al., 2000). High bone density was associated with an increased progression of knee OA when knee OA already present and characterised by osteophytes (Hannan et al., 1993; Zhang et al., 2000).

2.6.2. Local Biomechanical factors

a) Obesity increases the load being transferred to the knee joint (Felson et al., 2000) where 60-70% of weight-bearing load is transmitted through the medial tibiofemoral joint in healthy individuals (Felson et al., 2002). A high body mass index (BMI) (over 30 kg/m²) was found to be a risk factor for knee osteoarthritis and progression of the disease (Yusuf et al., 2011). Research has shown that an increase in body weight by two units of BMI, in obese individuals with knee osteoarthritis, may increase the risk of disease progression by 50 % (Felson et al., 1993).

b) Previous joint injury: An anterior cruciate ligament injury and meniscal tears have been shown to increase the incidence of knee OA (Atkins et al., 2004) by altering load distributions within the damaged knee joint during walking (Doherty et al., 1983; Englund et al., 2004).

c) Cultural: It is a possibility that cultures requiring kneeling or squatting activity over a long period, which is very common in some societies such as the Kingdom of Saudi Arabia, increase the risk of knee OA (Frontera et al., 2006).

d) Occupational: occupations which involve lifting or climbing stairs increase the incidence of knee OA and the disease process by increasing the load on the knee joint (Jensen, 2007). Sports persons and young people doing exercises also face the issue of osteoarthritis because these activities require more direct joint impact and joint twisting (Pujari & Alton, 2010). Evidence concluded that highly intensive sports, such as weight-lifting and soccer increase the risk of knee OA (Driban et al., 2015), One of the potential reasons for this is that the cumulative loading on the knee joint is increased (Klussmann et al., 2010).

e) Muscle weakness: Decreasing muscles strength, especially in the quadriceps and gluteus medius muscles (Chang et al., 2005): Slemenda et al. (1998) found that quadriceps muscle

weakness increases the development of knee OA, and this weakness has been noticed in individuals with knee OA compared to healthy individuals (Messier et al., 1992; Lewek et al., 2004a). Muscle weakness may due to presence of pain during knee joint movement (Felson et al., 1987) lead to reduced ability of muscle around knee joint to absorb forces during movement resulting in greater loads on the knee joint (Selmenda et al., 1998).

f) Varus malalignment: The risk of further narrowing of joint space occurs 3 - 4 times more often with the presence of varus malalignment in individuals with knee OA (Sharma et al., 2001). Therefore, increasing varus malalignment is associated with the progression and development of knee OA (Brouwer et al., 2007).

These risk factors are multi-factorial and cause degenerative changes within the tissues surrounding the knee. When these changes occur, dynamic balance impairments is associated with knee OA.

2.7. Balance in individuals with knee osteoarthritis

The inability of a body to maintain a stable base of support during movement or physical activity is known as dynamic balance deficits (Gribble et al., 2004 & 2012). Dynamic balance deficits appear in individuals with knee OA (Hinman et al., 2002), and have been shown to be a risk factor for falls in elderly (Stalenhoef et al., 2002). Balance control is affected by various components such as physiological changes in the neuromuscular system (muscle weakness), aging process, sensory system (reaction time), and proprioception impairments (Skinner et al., 1984; Doherty et al., 1993; Stevens et al., 2008; Muir et al., 2010). These components are found in individuals with knee OA (Lin et al., 2009).

Hinman et al., (2002) compared between individuals with knee OA with an age-, gender- and body-mass-matched group to assess static and dynamic standing balance. They found that participants in the knee OA group demonstrated poor dynamic standing balance and there was a significant difference between the knee OA group and healthy group using step test ($p < 0.0001$). Therefore, dynamic balance impairments are used to distinguish between patients with knee OA, unilateral and bilateral knee OA (Hinman et al., 2002), to predict the lower extremities injury (Bennell et al., 2003; Plisky et al., 2006; Herrington et al., 2009) and to demonstrate improvement from interventions (Lim et al., 2008; Bennell et al., 2010). In addition, individuals with knee OA demonstrated greater body sway in anterior-posterior and lateral directions compared to healthy group using sway-meter (Hinman et al., 2002). However, static body sway is common method has been used in studies to

evaluate static balance deficits using force platforms (Kollegger et al., 1992), no statistically significant differences were seen between groups (Hinman et al., 2002). Therefore, the body sway unable to detect static standing deficits in individuals with knee OA (Hurley et al., 1997).

An important aspect must be considered with individuals with knee OA is that falls and loss balance during activity which are common in individuals with knee OA (McAlindon et al., 1992; Fitzgerald et al., 2004; Mackenzie et al., 2012), and therefore static standing balance is potentially less able to identify individuals at risk due to balance impairments compared to dynamic test (Shumway-Cook et al, 1997 & 2000; Mackenzie et al., 2012).

Therefore, there is a need for an appropriate instrument to assess the dynamic balance in individuals with medial knee OA and to determine any change in their balance after the intervention.

2.7.1. Step Test

The step test (ST) is a commonly used method to measure dynamic balance in knee OA (Hinman et al., 2002; Bennell et al., 2010). This test is inexpensive, easy to perform, and reliable in old adults (Hill, 1996). The number of times the participants could step their foot up and down is the outcome of this test. The participants are instructed to maintain their balance on single limb while stepping the contralateral limb up and down on 15 cm high step as quickly as possible for 15 seconds. The ST was developed as a dynamic balance test for post-stroke patients (Hill, 1996).

The ST has shown that the number of steps in 15 seconds significantly decreased in individuals with knee OA (12 steps) compared to a healthy control group (17 steps) using the ST (Hinman et al., 2002). However, the ST would only assess dynamic standing balance in one direction (anterior) and neglects the distance between the standing base and the 15 cm high step that may play a vital role in body stability during the movement. However, the ST assesses the individuals stepping their foot as fast as they can to evaluate their balance and thereby it is a test of endurance rather than functional balance. Additionally, to our knowledge, there is no gold standard instrument to measure dynamic balance and ST was developed to use with upper motor neuron lesion such as stroke patients thereby his reliability was proven with this particular population (Hill, 1996; Hong et al., 2012). As a result of this, an appropriate method to measure dynamic balance in individuals with knee OA is needed.

2.7.2. Star Excursion Balance Test

The star excursion balance test (SEBT) is a simple, inexpensive test, used to measure dynamic balance (Gribble et al., 2012) that incorporate a single-leg stance with maximum reach of the other leg (Olmsted et al., 2002). It is performed by measuring a maximal distance that will be reached by

using one leg in different directions, and then return slowly to starting position (double support) with keeping balance throughout the test (Olmsted et al., 2002; Gribble et al., 2007). The directions relative to the support leg on the platform; anterior (A), anterolateral (AL), anteromedial (AM), posterior (P), posterolateral (PL), posteromedial (PM), medial (M), lateral (L), and difference between them equal 45˚(Olmsted et al., 2002). The SEBT is used in clinics and laboratories and it can be performed quickly and easily to help the researcher determine if the participant has returned to normal condition or has achieved any progression after intervention (measuring the effectiveness of the intervention) (Gribble et al., 2012). However, the length of protocol is the disadvantage of this test. Evidence has recommended doing four practice trials following by three test trials in each of the eight directions because the learning effect was found in the first four trials (Robinson and Gribble, 2008a; Munro and Herrington, 2010).

The reliability of SEBT is proven in many studies to measure dynamic balance in healthy subjects (Kinzey and Armstrong, 1998; Hertel et al., 2000; Munro and Herrington, 2010), and to assess dynamic balance in patients with musculoskeletal conditions such as chronic ankle instability (Hertel et al., 2006) or anterior cruciate ligament tears (Herrington et al., 2009).

Focusing the assessment on specific directions that are that performed by certain muscles is a potential method to reduce the time (Olmsted et al., 2002; Herrington et al., 2009), and these certain muscles are significantly activated than other muscles in eight directions (Early and Hertel, 2001). The medial, anteromedial, and posteromedial directions are recommended to test with chronic ankle instability because these directions were the most affected compared to healthy population (Hertel et al., 2006). Whereas, the anterior, lateral, medial, and posteromedial are recommended to test with anterior cruciate ligament tears because dynamic balance was significantly decreased in these directions compared to healthy population (Herrington et al., 2009). In knee OA, the anterior and medial directions will be proposed to test because quadriceps muscle and gluteus medius muscle are affected with knee OA and become weak (Slemenda et al., 1997; Chang et al., 2005). The directions relative to the support leg on the platform. Anterior (A), medial (M) directions are the most relevant to knee OA condition However, test-retest reproducibility of the SEBT has not been investigated in individuals with knee osteoarthritis (OA).

While an understanding of balance is important, the progression of knee OA has been postulated to be a dynamic disease once an individual in one the pathway (Baliunas et al., 2002). Therefore, an understanding of the normal dynamic walking patterns and biomechanical changes in knee OA need to be appreciated to gain a full understanding of preventable options.

2.8. Normal gait characteristics and knee OA

The gait is defined as the rhythmic alternating movement of the limbs of the lower extremity which lead to the forward movement of the body. The gait cycle is the activity that starts from heel strike of one foot to the heel strike of the same foot (Wang et al., 2012). When looking at walking, the gait cycle is divided into two main phases: stance phase which comprises four stages, early-stance (0%–20% of the gait cycle), mid-stance (21%–40% of the gait cycle), and late-stance (41%–60% of the gait cycle), in addition to the swing phase (61%–100% of the gait cycle) (Mündermann et al., 2004). The stance phase and swing phase can also be divided into eight functional phases; initial contact, loading response, mid stance, terminal stance, pre-swing, initial swing, mid-swing and terminal swing (Perry and Davids, 1992; Vaughan et al., 1999) (Figure 2-4) but generally in knee OA literature the role of early, mid and late-stance are more appropriate (Jones et al., 2013a).

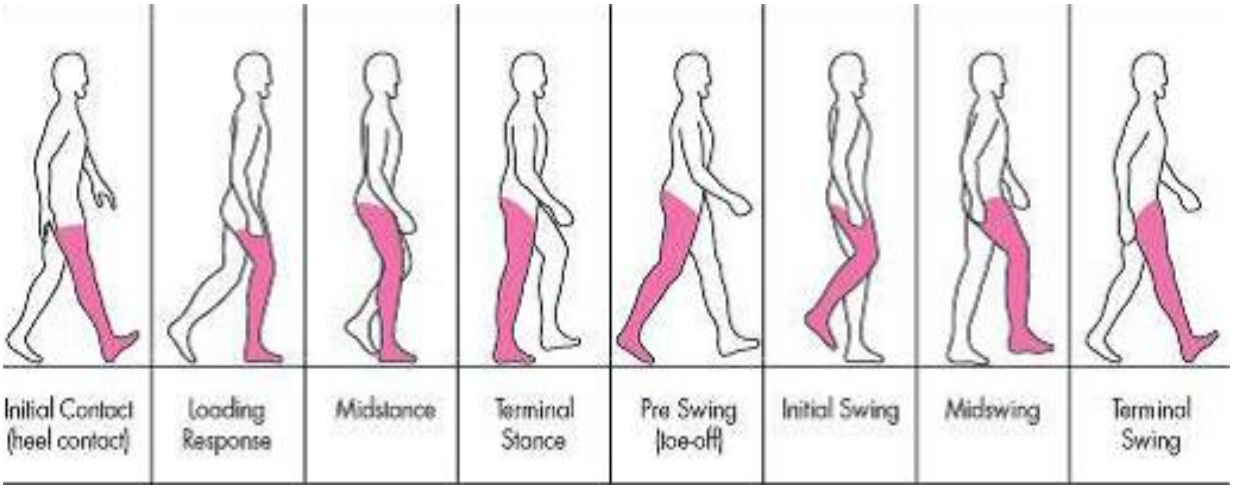


Figure 2-4: Phases of the normal gait cycles, right limb is the reference. (http://keywordsuggest.org/gallery)

The stance phase of gait is the period of time during which the foot is in contact with the ground. This is the weight-bearing phase of gait and provides body stability, approximately 60% of the gait cycle. The swing phase of gait is period of time during which the foot is off the ground and swing forward to provide forward momentum of the limb, approximate 40% of the gait cycle (Mary, 1988).

2.9. Biomechanics of medial knee osteoarthritis

As stated earlier (section 2.5), the medial tibiofemoral compartment is ten times more frequently affected than the lateral tibiofemoral compartment by OA (Ahlback, 1968). This may be explained by the fact that medial tibiofemoral cartilage is exposed to a greater load than lateral tibiofemoral cartilage (Andrews et al., 1996). Additionally, a roughly 2.5 times greater load is found on the medial tibiofemoral joint compared to the lateral tibiofemoral joint during walking (Schipplein and Andriacchi, 1991) due to the ground reaction force (GRF) passing medially to the knee joint. (Figure 2-5) where GRF is the force that generated when the foot contacts the ground (Lelas et al., 2003).

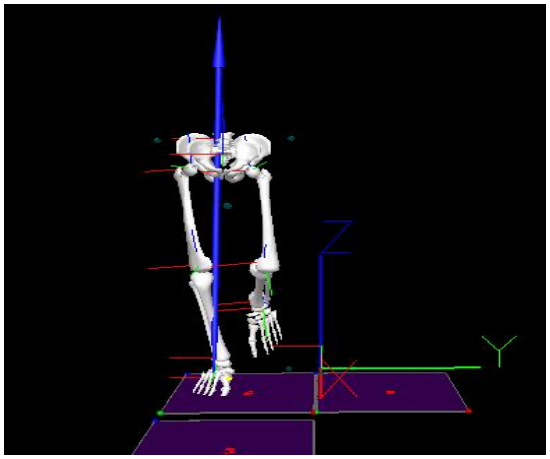


Figure 2-5: Blue arrow indicates to the Ground Reaction Force vector during gait

GRF may be an indication of the load on the medial tibiofemoral joint, and a strong correlation was found between high GRF and body mass and rapid acceleration (Felson et al., 2000; Lelas et al., 2003). A higher ground reaction force and higher joint moments may result of high acceleration of the centre of mass of the body and individuals, in general, individuals experiences a higher knee loading during fast walking. Therefore, individuals with medial knee OA walk slower than healthy people leading to reduce knee loading (Robon et al., 2000; Mündermann et al., 2004),

Knee alignment (referred to as the mechanical axis or the hip-knee-ankle angle) in the frontal plane has been associated with the distribution of the load between the medial and lateral tibiofemoral joints and is measured as the angle formed by the intersection of the line connecting the hip centre to the knee centre with the line connecting the knee centre to the ankle centre (Cook et al., 2007).

The mechanical axis range from -9˚ to +15˚, the negative indicates the varus direction whereas the positive indicates the valgus direction (Moreland et al., 1987).

In healthy individuals, 60-70% of the weight-bearing load is transmitted through the medial tibiofemoral joint (Felson et al., 2002) because the mechanical axis passes medially to the knee joint creating a 1˚ varus knee alignment (Moreland et al., 1987). In individuals with medial tibiofemoral OA, the mean varus knee alignment was 7.2˚ ± 4.8˚, which is considered significantly higher compared to healthy individuals (Cooke et al., 1994). Chang et al., (2015) reported that a mean knee mechanical axis at baseline was 4° in individuals with medial knee OA. Moreover, varus knee alignment was higher in individuals with moderate-to-severe knee OA by 2˚ to 6˚ compared to individuals with mild knee OA (Hurwitz et al., 2002). Varus malalignment (varus knee alignment) is associated with tibia cartilage loss in individuals with medial tibiofemoral OA (Sharma et al., 2008). In knee OA groups, disease severity becomes worse with increasing varus knee alignment (Hurwitz et al, 2002; Wada et al; 2002; Mündermann et al., 200). Therefore, progression of the medial knee OA may be delayed by reducing the varus knee alignment (Teichtachl et al., 2009) and the EKAM (Miyazaki et al., 2002). The following will review the differences between individuals with medial knee OA and healthy individuals during gait, namely temporal-spatial parameters, kinematics and kinetics.

2.9.1. Temporal-spatial variables (timing and distance) in medial knee OA

Timing and distance gait variables are measured in individuals with knee OA during gait to identify abnormal changes that may attempt by the patients to diminish the symptoms or to reduce the loading on the affected knee joint. Altered timing and distance variables are seen in individuals with knee OA and are easily obtained with minimal interference with individuals and very low cost.

Walking speed in individuals with knee OA is significantly reduced compared to healthy individuals (Al-Zahrani and Bakheit, 2002). In individuals with knee OA, a decreased walking speed was correlated with decreased stride length, decreased cadence, and increased double limb support time (Landry et al., 2007; Astephen et al., 2008a). Patients use these strategies to reduce the load on the knee joint (Winter, 1991), decrease knee pain (Al-Zahrani and Bakheit, 2002), and increase stability of the knee joint by increasing stance time (Schmitt and Rudolph, 2007). In addition, as walking at faster speed may result in a higher knee loading, reductions in walking speed lead to reductions in knee joint loading (Mündermann et al., 2004).

2.9.2. Kinematic and kinetic parameters in medial knee OA

During early stance, decreased peak knee flexion angles and decreased peak hip flexion angles have been associated with knee OA compared to healthy subjects (Kaufman et al., 2001; Messier et al., 1992; Landry et al., 2007). Moreover, these reductions were reported on the affected side compared with the contralateral side in individuals with unilateral knee OA (Briem and Snyder-Mackler, 2009). Evidence has shown the knee flexion angle was reduced in moderate and sever knee OA compared to healthy subjects (Al-Zahrani and Bakheit, 2002; Astephen et al., 2008b) (Table 2-1).

Table 2-1: Asymptomatic and OA discriminant analysis summary (Astephen et al., 2008a).

Measure	**interpretation**
Hip flexion angle	OA had lower hip flexion angle compared to healthy.
Knee flexion angle	OA had lower knee flexion angle in loading and swing compared to healthy.
Ankle flexion angle	Sever OA had higher ankle plantarflexion angle in early stance and lower dorsiflexion in late stance in pre-swing compared to healthy.
Hip flexion moment	Sever OA had lower early stance and swing and higher in mid-stance compared to moderate.
Knee flexion moment	Severe/moderate OA had smaller in early and late stance compared to healthy.
Ankle flexion moment	Severe OA had greater ankle dorsiflexion moment in early stance and small ankle dorsiflexion moment in late stance compared to healthy.
Ankle internal rotation moment	Severe OA had lower ankle internal rotation moment in early stance and higher in late stance compared to moderate OA.
Hip internal rotation moment	OA had lower hip internal rotation moment in stance compared to healthy.
Hip adduction moment	OA had higher hip adduction moment in mid-stance and lower in late stance compared to healthy.
Knee internal rotation moment	Moderate OA had higher knee internal rotation moment in late compared to healthy.
Knee internal rotation moment	Severe OA had smaller knee internal rotation moment in stance compared to healthy.
Knee adduction moment	OA had higher knee adduction moment in mid-stance compared to healthy.

Normally during early stance, and if isolating the role of soft tissues as absorbers, the knee joint plays an important role in absorbing the shock which results in knee flexion at initial contact of roughly 15° during walking and the degree of knee flexion angle increases with faster acceleration for extra shock absorption (Winter, 1991); However, individuals with knee OA cannot adopt this strategy because of the reduction in knee flexion angle (Creaby et al., 2012). This may be explained by muscle weakness (especially quadriceps muscle) (Fisher et al., 1997; Chang et al., 2005), the compensatory strategy attempted in the presence of knee instability (Schmitt and Rudolph, 2007),

and knee pain (Kaufman et al., 2001). Sagittal plane range of motion (ROM) at hip, knee, and ankle was significantly reduced with severe knee OA compared to moderate knee OA (Astephen et al., 2008b) and healthy participants (Al-Zahrani and Bakheit, 2002) as these reductions in ROM are more likely to be compensatory gait responses to knee pain. Gok et al., (2002) found that knee adduction angle increased during stance in individuals with medial knee OA. An increased knee adduction angle at initial contact has been shown in individuals with knee OA (Briem & Snyder-Mackler, 2009; Creaby et al., 2012) and has been related to disease progression in medial knee OA (Miyazaki et al., 2002). Possibly due to morphological changes in medial compartment of the knee joint result in disease such as cartilage volume loss, loss joint height (narrowing), and meniscal damage, greater knee adduction angle occurs. Higher knee varus angle shifts the loading-bearing axis medially to the centre of the knee joint, increasing a moment arm that creates forces across the medial compartment of the knee joint and concurrently stretches the soft tissues on the lateral compartment. This mechanism leads to unload the lateral compartment by lifting the lateral epicondyle (Schipplein and Andriacchi, 1991; Andriacchi, 1994).

Medial knee OA is a mechanical disease affected by the intensity and magnitude of the load on the medial compartment of the knee joint (Brandt et al., 2008). In healthy individuals, 60-70% of the weight-bearing load is transmitted through the medial tibiofemoral (Felson et al., 2002), this may be due to a stance phase knee adduction moment, greater load passes medially than laterally to the centre of knee joint even in healthy knee, neutrally aligned (Hurwitz et al., 2002).

Kaufman et al (2001) found that the knee extension moment was lower in individuals with knee OA compared to healthy individuals. Astephen et al., (2008a) found that ankle flexion moment was higher in mid-stance and lower in late-stance in individuals with severe knee OA compared healthy individuals. During early stance, smaller knee flexion and knee extension moments appeared with moderate and sever knee OA compared with healthy knee (Astephen et al., 2008a). In addition, lower hip flexion moment and hip external rotation moment have been found with knee OA (Al-Zahrani and Bakheit, 2002; Astephen et al., 2008a).

Astephen et al., (2008b) found that the hip adduction moment was lower during the stance phase in individuals with knee OA compared to healthy subjects. This finding supports those of Chang et al (2005) and Mündermann et al (2005) who found that a lower hip adduction moment was found in participants with knee OA and that it has been associated with progression of knee OA.

Individuals with knee OA had lower hip extension moment during late stance (Mündermann et al., 2005; Huang et al., 2008). For the frontal plane, the EKAM has been found to be higher in individuals with knee OA (Astephen et al., 2008b). Moreover, individuals with medial compartment

OA have a higher knee adduction moment during mid-stance, decreased peak of knee flexion moment and a higher hip abduction moment during late stance (Astephen et al., 2008a).
Therefore, knee joint loading is important to further understand the disease process and prevention and to alter this loading in knee OA that has been associated with knee OA.

2.9.2.1. External knee adduction moment

The external knee adduction moment (EKAM) is a surrogate measure of medial knee load during gait (Schipplein and Andriacchi, 1991). During gait, in individuals with medial knee OA, the line of the ground reaction force (GRF) passes more medially to the knee centre, thereby the moment arm increases and the GRF causes the tibia to shift into the varus position (Figure 2-6).

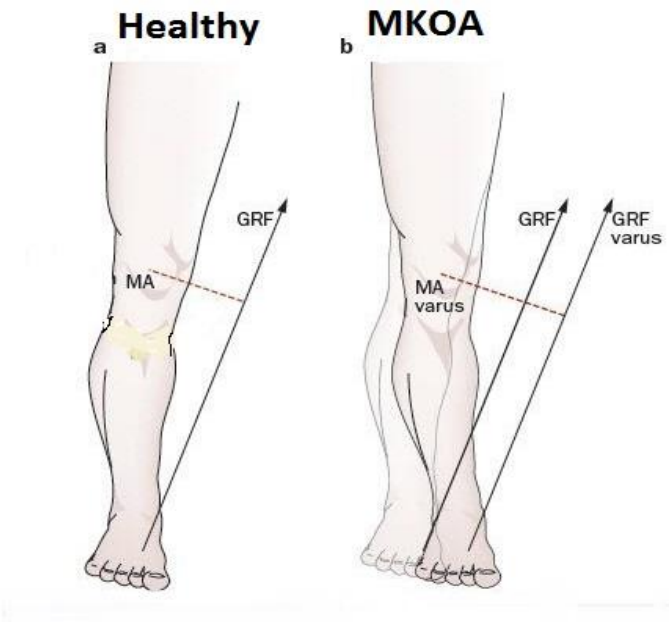


Figure 2-6: Ground reaction force vector location and moment in (a) healthy (b) medial knee OA (Reeves & Bowling, 2011).

This results in increased loads on the knee joint across the medial compartment, as indicated by a high external knee adduction moment (EKAM) (Hinman et al., 2013). The EKAM is considered a surrogate measure of medial compartment load. Moreover, a higher EKAM at baseline could predict radiographic knee OA and is associated with an increased rate of disease progression (Miyazaki et al., 2002; Thorp et al., 2006). In knee OA, varus knee alignment (mechanical axis) was the best

single predictor of the peak adduction moment during the stance phase (Hurwitz et al, 2002; Barrios et al., 2009a) as mentioned in section 2.9. Additionally, varus knee alignment has been found to be high in individuals with medial knee OA (Sharma et al., 2001; Tanamas et al., 2009). A higher correlation was found between varus knee alignment and peak knee adduction moment during walking in individuals with medial knee OA (Hurwitz et al, 2002). Therefore, reducing the varus knee alignment lead to EKAM reduction and thereby might delay the progression of medial compartment OA of the knee joint (Miyazaki et al., 2002; Teichtahl et al., 2009). Dynamic varus knee alignment was 6.4˚ during the first half of stance whereas during the second half of stance it was 4.6° in individuals with medial knee OA compared to healthy participants (Kumar et al., 2013) and therefore, the knee loading has been found higher with medial knee OA (Jones et al., 2014).

The EKAM curve consists of an early stance peak EKAM (0 – 20 % of gait cycle), trough (21-40% of gait cycle) and late stance peak EKAM (41 – 60% of gait cycle) during the stance phase. The early stance peak (1st peak) is commonly measured to determine the amount of load on the medial compartment of the knee joint during gait (Hurwitz et al., 2002; Mündermann et al., 2005). Early stance EKAM has been found to be higher in individuals with mild, moderate, and severe knee OA compared to healthy subjects (Kaufman et al., 2001; Rudolph et al., 2007) and has been linked with severity and progression (Miyazaki et al., 2002). Moreover, the EKAM has been found to be significantly higher at trough (mid-stance) in individuals with mild, moderate, and severe medial compartment OA compared to healthy participants. Mid-stance peak EKAM was higher than early peak EKAM in some studies (Landy et al., 2007; Astephen et al., 2008b). Moreover, patients with mild, moderate, and severe medial tibiofemoral OA have a higher late stance peak (2nd peak) compared with healthy subjects (Astephen et al., 2008b, Huang et al., 2008). Therefore, assessing the EKAM throughout stance phase gives insightful understanding of knee loading.

Risk of presence and progression of medial knee osteoarthritis is associated with increased loading on the medial knee joint during gait (Andriacchi and Mündermann, 2006) and disease severity is increased with a higher EKAM (Sharma et al., 1998; Miyazaki et al., 2002; Hurwitz et al., 2002; Thorp et al., 2006; Landry et al., 2007; Huang et al., 2008; Bennell et al., 2011a). Thus, the external knee adduction moment has been shown to be a strong indicator of the onset and progression of medial knee osteoarthritis, and to slow the progression of the disease in the knee joint (Bennell et al. 2011a, Chang et al., 2015), the EKAM reduction must be achieved (Miyazaki et al., 2002).

Miyazaki et al., (2002) showed that the EKAM significantly increased in patients with progression of knee OA compared to patients without disease progression, after six years follow-up. They reported that the risk of progression of knee OA increased 6.46 times when the EKAM increases by

1% on the 1st peak (Miyazaki et al., 2002). A high EKAM at baseline was associated with greater loss of cartilage volume in individuals with knee OA over two years follow-up (Chang et al., 2015).

However, whilst EKAM has been found to be an objective measure of medial compartment load and a high EKAM was strongly associated with great medial load on the knee joint and accelerate the progression of knee OA. Walter et al., (2010) showed that the effect of EKAM reduction did not always guarantee a reduction in medial compartment contact force due to a concurrent increase the knee flexion moment (KFM) and that this increase in the KFM may reduce the benefits of reducing the peak EKAM. In Walter et al., (2010) study, one participant with neutral knee alignment was recruited, whereas individuals with medial knee OA have a varus malalignment (Sharma et al., 2001), and therefore their findings cannot be generalised. A recent study investigated the effect of EKAM and KFM on cartilage changes over 5 years in sixteen subjects with medial compartment OA (Chehab et al., 2014). They found that the EKAM and KFM have a significant effect on the medial tibiofemoral joint, causing greater cartilage change but at two different sites. The EKAM has an influence on femoral cartilage while KFM has an influence on tibial cartilage. Therefore, the researchers have suggested that to achieve greater reduction in medial compartment load and may delay the progression of the disease in individuals with medial knee OA, both EKAM and KFM during walking must be considered (Walter et al., 2010; Chehab et al., 2014).

In contrast, in a large cohort study, 212 individuals with knee OA were recruited to assess EKAM, KFM, during walking and their relationship with medial tibiofemoral disease progression over two years (Chang et al., 2015). They found that the EKAM could measure medial knee load independently without any contribution from the KFM while the EKAM has a significant association with the progression of medial tibiofemoral OA. Additionally, they did not find a correlation between peak KFM and cartilage damage, joint space narrowing on the tibiofemoral compartment, medial femoral surface damage, or medial tibial surface damage during walking. However, a negative correlation was found between EKAM and knee flexion moment in nine individuals with instrumented total knee replacements, during ascending or descending stairs (Trepczynski et al., 2014). This may be explained by the fact that the individuals may have flexed their knee more during high flexion activities such as stair ascent and descent therefore the KFM increased. This correlation was not found during walking in individuals with medial knee OA when the EKAM was reduced by wearing lateral wedged insole (Jones et al., 2014)

Therefore, an increase in the KFM with EKAM reduction may be a compensatory increase which may not affect joint structure (Chang et al., 2015) or it may be due to high knee flexion activity (Trepczynski et al., 2014).

Different strategies have been observed in individuals with medial knee OA where they might be used as compensatory mechanisms due to the increased load on the knee joint. Individuals with knee OA tend to use these strategies to decrease the EKAM by altering their gait patterns, such as by increasing lateral trunk sway towards the affected stance limb during walking (Mündermann et al., 2005; Hunt et al., 2008), decreasing walking speed with shorter stride length (Andriacchi, 1994), increasing foot progression (toe-out) angle during stance phase (Chang et al., 2007; Jenkyn et al., 2008), or altering foot and ankle position (Pazit et al., 2010). A short review of these will now be presented.

Lateral trunk sway towards the affected stance limb

Evidence has shown that the EKAM might be reduced by 65% during gait increasing lateral trunk lean towards the side of the weight bearing which can displace the centre of mass (COM) more laterally(Hurwitz et al., 2002; Hunt et al., 2008). As depicted in Figure 2-7, the line of GRF is displaced closer to the centre of knee joint lead to decreasing the length of moment arm (distance between line of GRF and centre of knee joint) (see section 2.9.2.1) (Hurwitz et al., 2002; Mündermann et al., 2005; Hunt et al., 2008) .

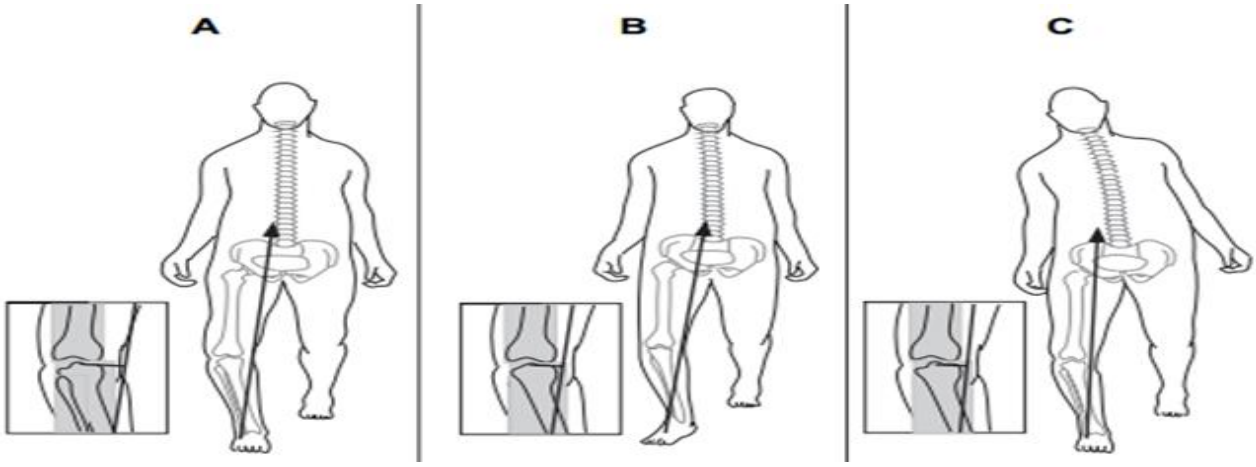


Figure 2-7: (A) Distance between GRF and knee joint centre in knee OA during gait. (B) Distance between GRF and knee joint centre in knee OA during gait with toe-out. (C) Distance between GRF and knee joint centre in knee OA during gait with leaning the trunk. (Hunt et al., 2008).

Moreover, the degree of lateral trunk lean was increased in individuals with severe knee OA compared to mild knee OA (Hunt et al., 2008). Therefore, increasing lateral trunk lean has been recommended as a compensatory mechanism to decrease the EKAM in knee OA (Mündermann et

al., 2008). Radebold et al (2000), however, stated that a typical trunk movement with activity (e.g. walking) can protect the back from injuries and back pain. Therefore, doing this strategy repetitively might increase the risk of back injury, back pain, or falls in individuals with or without knee OA (Radebold et al., 2000; Rogers and Mille 2003).

Walking speed and stride length

Temporal, spatial, kinematic, and kinetic parameters are correlated with variance in walking speed in individuals with or without knee OA. For example: walking at a fast walking speed was associated with decreased stride time, increased stride length, increased ROMs and angles in hip, knee, and ankle in the sagittal plane, and the EKAM becomes higher as well (Al-Zahrani and Bakheit, 2002; Kaufman et al., 2001; Mündermann et al., 2004; Lewek et al., 2004; Childs et al., 2004; Thorp et al., 2006; Rudolph et al., 2007; Schmitt and Rudolph, 2007; Landry et al., 2007; Astephen et al., 2008a; Zeni & Higginson, 2009; Creaby et al., 2012). In addition to what is mentioned in sections 2.9.1, walking speed is highly correlated with EKAM, where the faster the walking speed is, the higher the EKAM will be. Therefore, evidence has shown that walking at a slow walking speed with decreased stride length is common in individuals with medial knee OA as a compensatory mechanism to reduce the EKAM and thereby reduce the medial compartment loads (Kaufman et al., 2001; Mündermann et al., 2004).

Altering foot position

Altering the foot position displaces the line of GRF closer to or away from the knee centre, where the EKAM is affected by altering foot position during walking. Individuals with knee OA tend to alter foot position by pronate their feet to enable the foot to be plantigrade when weight-bearing (gait) compared to healthy individuals (Riegger-Krugh & Keysor, 1996; Levinger et al., 2010; Pazit et al., 2010). This strategy has been considered as a compensatory mechanism (responses to varus knee alignment) to reduce medial compartment loading, as it shifts the line of GRF laterally nearer to the knee centre, reducing the EKAM (Levinger et al., 2010).

Foot progression (toe-out) angle

Toe-out angle is formed by the angle between a line that is drawn from mid heel to the head of the 2nd metatarsal and the forward progression line of the body. Foot progression angle during walking is an important factor in changing the magnitude of medial compartment load, as increasing toe-out angle has been found to reduce the magnitude of EKAM in knee OA (Jenkyn et al., 2008). This was identified as an adaptive strategy during gait to reduce the EKAM by altering the line of GRF

laterally so it is closer to the centre of knee joint, decreasing the moment arm length and thereby diminishing the load on the medial tibiofemoral joint (Hurwitz et al., 2002, Jenkyn et al., 2008). The greater toe-out angle strategy during walking has been found in individuals with knee OA to decrease the EKAM (Mündermann et al., 2008). Indeed, increasing toe-out angle affects the second peak EKAM rather than the first peak EKAM because this increase in angle occurs during the late stance phase, thus altering the line of GFR so that it becomes closer to the centre of the knee joint occurs in the late stance phase as well (Hurwitz et al., 2002). As a result of this, lower second peak EKAM is associated with increasing foot progression (toe-out) angle in individuals with knee OA (Jenkyn et al., 2008). An appropriate measure when conducting research on a knee OA population is the duration of the knee adduction moment in addition to the magnitude.

2.9.2.2. Knee adduction angular impulse

An additional measure of the load on medial tibiofemoral compartment is the knee adduction angular impulse (KAAI), which is defined as the magnitude and duration of the load on the medial knee compartment throughout the stance phase (the dark area under the adduction curve) (Thorp et al., 2006) (Figure 2-8).

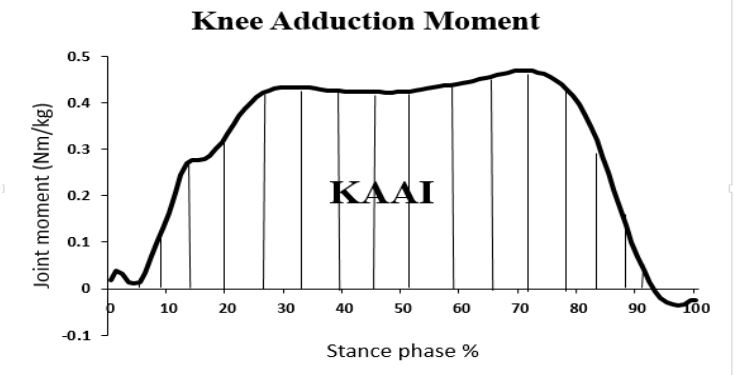


Figure 2-8: 1st and 2nd peaks and knee adduction angular impulse (KAAI).

Thorp et al (2006) was the first study, in osteoarthritis literature, that evaluated the KAAI in 117 patients with radiographic knee OA. Individuals with knee OA have a greater magnitude of the knee

adduction moment waveform and longer stance phase than the matched healthy group (Schipplein and Andriacchi, 1991; Al-Zahrani and Bakheit, 2002). This increases the knee adduction moment impulse in individuals with medial knee OA that considers the magnitude and duration of the load on the knee joint (Thorp et al., 2006). The KAAI is significantly higher in moderate knee OA compared to mild knee OA. The KAAI is more sensitive to distinguish between mild and moderate radiographic knee OA compared to the first peak of EKAM (Thorp et al., 2006). The possible reason is that walking speed is correlated with disease severity (Astephen et al., 2008b) with walking speed reducing incrementally with disease severity. Therefore, the amount of KAAI will increase if the speed reduced (stance time increased) and depends on the disease severity because a significant negative correlation was found between the KAAI and walking speed (Thorpe et al., 2006). The KAAI is partially dependent on the duration of stance phase. Whereas, the first peak of EKAM has been found to be higher in individuals with medial knee OA regardless of disease progression (Mündermann et al., 2005) and it increases when individuals (healthy or individuals with knee OA) walk at a fast speed. Moreover, KAAI at baseline has been shown to predict radiographic knee OA and is associated with an increased rate of disease progression (Bennell et al., 2011a; Chang et al., 2015).

A recent RCT by Bennell and colleagues in 2011 showed that baseline KAAI was associated with a greater loss of medial cartilage volume in 144 participants with medial knee OA after one year. They found that a higher KAAI was associated with the annual change in medial tibial cartilage thickness while (greater loss) no relationship between the first peak of EKAM and loss of medial tibial cartilage volume (Bennell et al., 2011a). In addition, Dore et al (2013) stated that cartilage lesion was been found in individuals with knee OA with high level of activity. Therefore, loss of cartilage volume may be explained by the high level of physical activity that the participants performed with sustained loading on the knee joint throughout one year, and therefore cartilage damaged. Additionally, cartilage volume loss (disease progression) strongly associated with the KAAI, which may represent cumulative loading on the medial compartment of the knee joint in the laboratory, rather than the first peak of peak EKAM (Bennell et al., 2011a); however, increasing joint space (disease progression) narrowing has been strongly associated with the first peak EKAM (Miyazaki et al., 2002). A large cohort study performed by Chang et al (2015) found that both peak EKAM and KAAI were associated with joint narrowing and cartilage loss over 24 months of follow-up, so continuous loading in the environment must be considered.

However, whilst the first peak EKAM and KAAI are common measurements from the laboratory, it is also necessary to determine an evaluation of the repetitive loading on the knee joint during free-living activity in this thesis.

2.9.2.3. Cumulative knee loading (CKL)

The majority of the research on knee OA focuses on the discrete value of the EKAM to measure the amount of loading on the tibiofemoral joint at a specific point only. Repetitive and excessive loading together are critical factors in the development and progression of knee OA, and therefore cumulative loading is a biomechanical approach that integrates the measures of abnormal loading on the tibiofemoral joint during physical activity to give an assessment of excessive and repetitive loading (Maly, 2008).

Cumulative knee loading (CKL) measures the total exposure to joint loading during physical activity. The CKL is calculated by measuring the mean of the normalised knee adduction angular impulse to body mass using three-dimensional gait analysis multiplied by one half of the mean number of steps per day that are taken by one leg using an accelerometer device (Actigraph, Fort Walton Beach, USA) (Robbins et al., 2009). The KAAI must be normalised to body weight for comparison with future studies.

Recently, one study has investigated the test-retest reliability of CKL in 30 healthy adults during physical activity (using the Actigraph monitor for seven consecutive days) (Robbins et al, 2009). They found that the CKL is a reliable measure of the total exposure to knee load (ICC ranged from 0.84 – 0.89). Maly et al., (2013) found that the cumulative knee load is nearly two times greater in individuals with knee OA compared to healthy subjects, and therefore it can be another way to distinguish between knee OA and healthy subjects, especially in intervention studies.

Individuals with knee OA are less likely to be active, more likely to, walk slower with a longer stepping time and lower cadence (Dunlop et al., 2011), and most likely to take fewer steps per day (White et al., 2014). Therefore, potentially, individuals with knee OA could produce higher CKL regardless of a lower step count because the load on the knee joint is still high. Indeed, CKL may be used to determine any change in the cumulative knee load in participants with knee OA after intervention by measuring knee adduction moment impulse during daily physical activity (total stepping).

Despite lower level of physical activity, individuals with medial knee OA would show a greater CKL because of higher medial knee loads than older healthy adults (Maly, 2008 & 2013). However,

there is no such study which has evaluated CKL in individuals with medial knee OA during an intervention period. Whilst knee loading is important in knee OA, the level of physical activity should be measured in individuals with knee OA. In order to be able to collect physical activity data during ambulation situation an appraisal of the literature in regards to activity in individuals with knee OA is needed but also to determine the best solution for data collection.

2.10. Physical activity

Physical activity is defined as any bodily movement produced by the musculoskeletal system that results in an expenditure of energy, such as household tasks, and has been classified into light, moderate, and vigorous intensity activity (Casperson et al., 1985), whereas physical function is defined as the ability to perform daily activities (Nelson et al., 2007). In individuals with knee OA, a negative correlation has been found between knee pain and movement. Therefore, individuals with knee OA may not be expected to be physically active as healthy individuals because of weight-bearing pain in knee joint increased during walking (Veenhof et al., 2012; Tonelli et al., 2011). In addition, there are wide range of factors that may affect the level of physical activity and act at individual, social, and environmental factors (Thibaud et al., 2012). Seefeldt et al (2002) states that some factors are fixed, for example, gender/sex factors while others are considered as modifiable, such as personality characteristics, and environmental factors (Seefeldt et al (2002). Age is negatively associated with total number of steps in individuals with knee OA ($r= -0.21(p=0.01)$) (Chmelo et al., 2014) as ages increases the number of steps decrease.

One of the measures from physical activity monitors are steps counts which are defined as the main component of walking activity (Paroczai and Kocsis, 2006), while the number of steps per minute (intensity of walking) is known as cadence (Abel et al., 2011). Running has the highest cadence with very low stance time, but running is unlikely to be performed by the majority of older individuals with knee OA (Novacheck, 1998; Paroczai and Kocsis, 2006).

Physical activity in adults has been classified by the number of steps taken ranging from low basal activity to high active, with the number of steps determining the range as shown in table 2-2 (Tudor-Locke and Bassett, 2004; Mitsui et al., 2008). Tudor-Locke et al., (2009) suggested that basal activity (stepping < 2500 steps/day) and limited activity (2500 – 4999 steps/day) are considered a sedentary behaviours or “sedentarism”.

Table 2-2: Classification of Physical Activity

Physical Activity	No. of Steps
Basal activity	< 2500 steps/day
Limited activity	2500 – 4999 steps/day
Low active	5000 – 7499 steps/day
Somewhat active	7500 – 9999 steps/day
Active	≥ 10,000 steps/day
Highly active	≥ 12,500 steps/day

(Tudor-Locke and Bassett, 2004; Mitsui et al., 2008; Tudor-Locke, 2009)

2.11. Level of physical activity in knee OA

Knee OA is highly prevalent in older individuals (Felson et al., 2000). Restriction of physical activity appears in 80% of knee OA patients and 25% of them cannot perform their major daily activities (WHO, 2003). Individuals may gradually lose their ability to walk faster over the years due to aging or diseases such as knee OA (Tudor-Locke et al., 2011b). Moreover, reduction in activity level (inactive behaviour- "sedentarism") is the main characteristic of individuals with knee OA, and sedentary time (time spent in sitting and lying position) increases in individuals with knee OA, as measured by actigraph (GT1M) (Dunlop et al., 2011).

Therefore, evidence suggests that a goal of 10,000 steps/day may not be suitable for older adults or some adults who are living with a chronic disease or disability such as hip or knee joint replacement, heart problems, or obesity (Tudor-Locke et al., 2009 & 2011a). In addition, taking 5,000 steps/day may be too much for some populations who are older and have a chronic disease that may limit their mobility (Tudor-Locke et al., 2011a), such as knee OA. Studies have reported that the range of steps taken in healthy younger adults was between 7,000 and 10,000 steps/day, while healthy older adults aged between 40 years-old and 69 years-old typically walked 6,000-7,000 steps/day (Bassett et al., 2000; Tudor-Locke et al., 2002; Tudor-Locke and Bassett, 2004).

A review of normative data (Tudor-Locke and Myers, 2001a) including studies published from 1980 to 2000 reported that healthy older individuals stepped between 6,000 and 8,500 steps/day while special populations (with chronic diseases) stepped between 3,500 and 5,500 steps/days. However, a recent review of normative data including studies from 2001 to 2009, reported that the healthy

older individuals walked between 2,000 and 9,000 steps/day while individuals with chronic disease that may limit mobility walked between 1,200 and 8,800 steps/day (Tudor-Locke et al., 2009).

From a knee OA perspective, a recent study investigated physical activity in 160 older adults with radiographic knee OA (Chmelo et al., 2014). They found that they stepped between 1459 and 15,949 steps/day and only 7.5% of them stepped over 10,000 steps/day. This may be because 10,000 steps/day are not suitable for individuals with knee OA. White et al., (2014), in a study of 1788 subjects, found that the typical daily steps counts for subjects with knee OA (majority of the individuals had tibiofemoral OA (> 54%) was > 6,000 steps/day using StepWatch3 attached to the ankle. Hurley et al., (2015) evaluated physical activity during one week in individuals with moderate knee OA compared to a matched healthy group using accelerometer (GT3X actigraph). They found that individuals with knee OA took fewer steps (mean= 6,518 steps/day) compared to healthy people (average steps = 8,367 steps/day) but there was no difference in sedentary time between the both groups. The accuracy of the actigraph in detecting any reduction in sedentary time may be one of the reasons (see section 2.13) (Kozey-Keadle et al., 2011; Lyden et al., 2012).

The reduction in activity level is mainly due to increased knee pain and the fear of falling during physical activity in older individuals (McAlindon et al., 1992; Fitzgerald et al., 2004). Cavanaugh et al., (2007) investigated the level of physical activity in 28 healthy older individuals and 12 disabled older adults who had functional limitations such as arthritis or joint replacement, using StepWatch3 for six consecutive days. They found that disabled older adults took fewer steps, had shorter period of activity (in minutes), and fewer bouts (a bout is defined as a sustained 10-second period of steps) of activity compared to healthy older adults. This lower level of activity may be explained by the high EKAM or the presence of knee pain.

Individuals with knee OA are considered inactive people who walk less than 5,000 steps/day; however, this value of stepping may increase in the absence of knee pain (Wideman et al., 2014, Chmelo et al., 2014; White et al., 2014). Rakel et al., (2012) suggested that knee pain during movement, such as 6-minute walk task, was a strongly correlated with clinical outcomes in individuals with knee OA. Moreover, individuals with knee OA commonly experience discomfort with joint movement (mainly during walking) due to knee pain, and this discomfort forces the individuals to limit their activity (Wideman et al., 2014). Wideman et al (2014) suggested that the majority of individuals with knee OA showed a sensitised response to routine activities such as walking. This may be explained by the exacerbation of knee pain during walking tasks (Van Damme et al., 2004; Goubert et al., 2004). Presence of knee pain may explain why individuals with knee OA spend a long time in sitting, lying and why they take fewer steps compared with healthy older

subjects (Cavanaugh et al., 2007). While individuals with knee OA walk slower and perform lower levels of activity, changing their behaviour have many benefits aspects.

2.12. Importance of physical activity in knee OA

Individuals with knee OA are particularly inactive and their health is at risk (Fontaine et al., 2004; Keysor, 2003) because of a reduced quality of life, muscle weakness, and weight gain (Visser et al., 2015) that increases loading on the knee joint (Felson 1992 & 2000), and may lead to accelerate the progression of knee OA (Miyazaki et al., 2002). Therefore, increasing the level of activity in individuals with knee OA has been recommended because of the health benefits (Nelson et al., 2007). Improving physical activity in individuals with osteoarthritis reduces mortality and the risk of incident of serious diseases such as obesity, cardiovascular disease, and hypertension (Pedersen et al., 2006). Evidence has shown that slow walking was highly associated with cardiovascular mortality in older individuals (Dumurgier et al., 2009).

Yasunaga et al., (2006) suggested that an increase of 2000 steps over baseline may be recommended for improved health-related quality of life (HRQoL) (McAlindon et al., 1992; Fitzgerald et al., 2004). Moreover, evidence has shown that weight loss in 142 older patients with knee OA in a diet trial study was associated with reduction in knee loading (1:4 times) (Messier et al., 2005) and increasing the activity level by 2,100 to 2,500 steps/day in obese subjects using behaviour modification programmes was associated with weight loss (Bravata et al., 2007). Therefore, reducing weight mass in individuals with knee OA by increase number of steps may lead to decrease the load on the knees and thereby the progression of knee OA may delay (Felson et al., 2000). However, using behaviour modification programmes and diet could be taken long time and costly to apply with individuals with knee OA and may be not suitable for all individuals.

Pedometer-based programmes (known as walk plus programmes or behaviour modification programmes) set daily step goals (in short bouts) and individuals are instructed to reach those goals (Bravata et al., 2007). The effect of increasing the number of steps in healthy older obese individuals using pedometer-based programmes was stated in the meta-analysis study by Richardson et al., (2008). Richardson et al., (2008) found that number of steps measured by a pedometer (SW-200) was increased in individuals by 1800 – 5400 steps/days leading to a reduction in their weight by approximately 0.05 kg/week. A higher number of steps (measured by a pedometer, Omron HJ-152K-E) was negatively correlated with changes in weight in women using pedometer-based programmes

(r= -0.6, p < 0.001) (Maturi et al., 2011). Although, pedometer-based programmes are useful to increase the steps counts, they are not a clearly articulated or detailed programme (Tudor-Locke et al., 2001b).

Evidence has shown that improving the level of activity by stepping more has several benefits for individuals; nevertheless, the high (>10,000 steps/day) and low (< 5,000 steps/day) level of physical activity is not recommended for individuals with knee OA (Dore et al., 2013; Kumer et al., 2014). Daily walking was measured in Dore et al., study (2013) at baseline using pedometer and cartilage loss was measured by using MRI at baseline and after 2.7 years. They found that stepping more than 10,000 steps/day was associated with a 1.32 to 1.52 times greater risk of cartilage lesions (Dore et a., 2013; Lin et al., 2013; Kumar et al., 2014). The authors concluded that individuals with knee OA should not step more than 10,000 steps/day (Dore et al., 2013) or doing high physical activity (Lin et al., 2013). This may be explained by the cumulative knee loading where stepping more than 10,000 steps/day or prolonged standing with sustained load on the knee joint. Only one study found that there was no association between high level of activity, measured by using StepWatch at the 60-month visit and structural changes using MRI at the 60 and 84-month visits in individuals with knee OA. This may be explained by the classification of level of activity in Øiestad, et al., (2015) study was different from the previous studies where they classified as low (<6,078 steps/day), moderate (6,078-7,938 steps/day), and high activity (>7,938 steps/day). However, the relationship existed between low level of activity and structured changes (Lin et al., 2013; Dore, et al., 2015) where low level of walking may result in limited joint compression that may provide insufficient stimulation of knee cartilage (Lin, et al., 2013).

Individuals with knee OA who stepped < 5,000 steps/day developed functional limitations 2 years after baseline, and therefore, taking > 6,000 steps/day is seen as a protective influence in individuals with knee OA from functional limitations. Moreover, increasing the number of steps by 1,000 steps/day in individuals with knee OA was associated with a 16% to18% lower risk of developing functional limitation (White et al., 2014).

In conclusion, the typical daily steps count for individuals with knee OA is more than 6,000 steps/day and it is recommended that individuals with knee OA walk between 5,000 to 10,000 steps/days to improve level of activity, reduce weight, decrease risk of functional limitation, decrease loading on knee joint, reduce risk of cartilage lesion, and improve their QoL. Therefore, level of physical of activity should be measured accurately during intervention in individuals with knee OA. However, it should not only characterise the stepping activity but also the other behaviour aspects such as standing and sedentary times which are considered as weight-bearing activity.

2.13. Measurement of physical activity in knee OA

As noted in the previous sections, studies have reported differences in the level of physical activity among individuals with knee OA and healthy older people due to the effect of the disease. In addition, intervention might increase the level of activity of individuals with medial knee OA, and thereby allow individuals to walk more and thereby disease progression increase. Moreover, increasing of physical activity may diminish the clinical effect of intervention on knee pain in individuals with knee OA. Therefore, reliable and accurate instruments to measure physical activity and number of steps pre- and post-intervention are needed.

Various methods have been used to measure physical activity and number of steps in individuals with knee OA. First, direct observation (video observation) is considered a gold standard instrument; however, it cannot be used outside the laboratory (Arem et al., 2015). In addition, direct observation cannot measure physical activity in free-living environments where physical activity naturally occurs. Therefore, strengths and limitations of questionnaires, pedometers, and accelerometers will be discussed below.

Questionnaires are subjective self-report measures of level of physical activity and cover most of the activities that are performed by the individuals during a previous period of time. These questionnaires are designed depending on age, conditions, culture, and the kind of activity (Taraldson et al., 2011; Ainsworth et al., 2015). Questionnaires are quicker, easier to administer, and less expensive to use in a large population compared to pedometers (Bassett et al., 2000) or accelerometers (Kriska and Caspersen, 1997). However, they have been found to have low-to-moderate validity for measuring sedentary behaviour (Atkin et al., 2012).

Questionnaires have been shown to overestimate measured activity level in older individuals (Irwin et al., 2001), and therefore they are unreliable (Washburn and Montoya, 1986). In addition, self-report questionnaires do not reflect the actual activities of patients with knee OA. So, questionnaires cannot accurately determine the sedentary time (Atkin et al., 2012). Another limitation to using self-report questionnaires of activity level is that culture and age might influence the validity of activity questionnaires (Taraldson et al., 2011). In addition, recall questionnaires are influenced by human memory, which may be weak in older individuals (Shephard, 2003).

Finally, although questionnaires have weaknesses, evidence recommends measuring the level of activity by using accelerometer alone or in combination with questionnaires (Terwee et al., 2011). The Human Activity Profile (HAP) and Physical Activity Scale for Elderly (PASE) are widely used

in research studies to measure the level of physical activity (Bilek et al., 2000; Bennell et al., 2004; Chmelo et al., 2013). The HAP is a self-report questionnaire measure of energy expenditure or physical fitness with 94-items. It has been widely used in both healthy and diseased populations, although the correlation between HAP and pain (WOMAC) was weak (r=0.18) (Bennell et al., 2004).

The PASE is commonly used with older adults to measure activity and can be used alongside pedometers or accelerometers to make a study stronger (Dinger et al., 2004; Chmelo et al., 2013). A significant correlation was found between PASE and accelerometer, actigraph, (r=0.91) (Dinger et al., 2004). The potential reason behand that is that the PASE can measure some activity that pedometers or accelerometers cannot measure, such as swimming (Figure 2-9).

"Q5. Over the past 7 days, how often did you engage in strenuous sport or Recreational activities such as jogging, swimming, cycling, singles tennis, aerobic dance, skiing (downhill or cross country or other similar activities?

Q5a. What were these activities?

Q5b. On average, how many hours per day did you engage in these strenuous activities?"

Figure 2-9: Part of the PASE that asking about the swimming activity

PASE is simple, easy to score, can be used with a large sample size, and has been designed to evaluate physical activity level of older adults during a week (Washbum et al., 1999). The reliability of PASE ranges from 0.69 to 0.80 in healthy older individuals (Washbum et al., 1993). Moreover, PASE was found to be valid and reliable (ICC= 0.91) for measuring physical activity, as there was a significant correlation with the accelerometer (Actigraph) $r = 0.43$ ($p < 0.01$) in 55 healthy older individuals (Dinger et al., 2004).

The PASE score combines information on light, moderate, and vigorous levels of activity during occupational, household, and leisure activities. Level of physical activity has been classified according to PASE scores into high level of physical activity (PASE > 242 points), moderate level of activity (PASE 124-242 points) and lowest level of activity (PASE 31-120 points) (Lin et al., 2013). A higher PASE score indicates a higher level of physical activity (Chmelo et al., 2013). The

level of physical activity in individuals with knee OA was ranged from 162-182 points in PASE score (Bennell et al., 2011b).

Pedometers are designed to detect stepping activity (Tudor-Locke et al., 2009) and are used widely in the literature to measure the number of steps in individuals with knee OA (Bennel et al., 2011b; White et al., 2013). Moreover, pedometers can measure the total activity level by measuring the time spent in walking or running (Backhouse et al., 2013). A traditional pedometer is placed on the waist and it depends on the vertical acceleration of the hip (up and down) to complete the electronic circuit in order to detect the steps (Tudor-Locke et al., 2009 & 2011b).

NL-1000 (New-Lifestyles Inc., Lees Summit, MO, USA), NL-2000 (New-Lifestyles Inc.), Kenz Life Order EX (Suzenken Co., Ltd, Nagoya, Japan), Omron HJ 720ITC (Omron Corp., Kyoto, Japan), SW-2000 (New Lifestyles Digi-walker SW-200, Yamax, Tokyo, Japan), and piezo-electric pedometers are the most common pedometers which use the same mechanism to measure the number of steps (Tudor-Locke et al., 2009 & 2011c).

Furthermore, pedometers are small devices, inexpensive, used widely, acceptable to the users, and used to measure number of steps, and total level of activity. However, they cannot measure quiet standing or low intensity activity (Rowlands et al., 2007) because they depend on the acceleration of the hip, which does not move during standing. Therefore, no movement occurs during standing for pedometers to detect and the researcher cannot measure the effectiveness of the intervention during changes in time spent in quite standing. Another disadvantage is that pedometers also cannot distinguish between upright position and sitting position (Backhouse et al., 2013) and thereby it is impossible to measure the time spent in a sitting position, and thereby it is impossible to detect any reduction in sitting time. The reason that they cannot detect sitting position is that they are designed to detect ambulatory activity using a vertical axis only (Tuder-Locke., 2009 & 2011c). A pedometer measures fast and normal walking speed (Murat et al., 2005), but it is less accurate for measuring slow walking (Ryan et al., 2006; Kinnunen et al., 2011). For example, it sometimes cannot detect walking (steps) when the person moves in crowded queue. The potential reason for this is that the hips do not move up enough to be detected by the pedometer. Moreover, the captured data might be affected by the pelvic tilt when placed it on the waist especially in obese and individuals with overweight (Swartz et al., 2003; Crouter et al., 2005).

Therefore, pedometers are not appropriate for measuring physical activity in older people who walk slower (Grant et al., 2008), in the inactive population (Kinnunen et al., 2011) and in obese

individuals (Felson et al., 2000). Those characterises which have been found in individuals with knee OA must be considered for choosing the instrument.

A recent systematic review recommended accelerometers for measuring the level of physical activity in individuals. However, the same reviews did not recommend any particular accelerometer to measure levels of physical activity in individuals with knee OA (Terwee et al., 2011; Veenhof et al., 2013).

Accelerometers: accelerometers were first used in the 1950s to measure the motion of human movement (Bao and Intille, 2004) such as RT3, StepWatch3, ActivPAL3 and Actigraph GTX. They can provide additional data such as cadence (steps per minute), time spent walking and number of steps (Grant et al., 2006). Accelerometers have other strengths in addition to their ability to measure number of steps and cadence; they can look at how much time is spent in standing position and sitting/lying, they can estimate energy expenditure during activity, and they can record activity over a long period (depending on the device). Additionally, accelerometers are small devices, light, and acceptable to the users (Grant et al., 2006). These devices are also relatively inexpensive. Most of these devices cannot distinguish between sitting and lying, and are not waterproof, so they cannot be used during water sports or when showering (Godfrey et al., 2008; Kozey-Keadle et al., 2011).

Accelerometers can be worn on the wrist, waist, thigh, or ankle and therefore, the location at which the accelerometers are placed, accelerometer orientation, and the kind of the physical activity being measured play a critical role in accuracy of the accelerometer and determining which device is appropriate for the study to collect the activity data. Although, accelerometers seem suitable devices to use, characteristics and the behaviour of individuals with knee OA should be considered to choose the appropriate for this population. The participants with medial knee OA are mainly older patients, who are inactive individuals (their activity behaviour is classified as sedentary behaviour), walk at slow walking speed, take few steps, and spend less time in activity (standing and walking times) (Cavanaugh et al., 2007, White et al., 2013).

Numerous monitors are available on the market for research studies include RT3, Actigraph, ActivPAL3, StepWatch3, AMP331, PAM, and Intelligent Device for Energy Expenditure and Physical Activity (IDEEA) Some of these monitors are sensitive to external movements, contain multiple sensors with cables, collect activity data for three days only, or are often used in laboratories such as the IDEEA monitor (Welk et al., 2007; Godfrey et al., 2008). The IDEEA monitor which comes with cables that may restrict the movement of individuals, and thereby it is difficult to wear

for a long time and in a free-living environment. While, the most common monitors, such as StepWatch3, RT3, AMP331, and PAM, measure number of steps, energy expenditure, distance, speeds, or step length (Godfrey et al., 2008), the actigraph and activPAL3 monitors can measure more data, such as time spent in different positions and quiet standing. Additionally, the activPAL3 monitors can measure sedentary time with high accuracy in comparison with the actigraph monitor (Kozey-Keadle et al., 2011; Lyden et al., 2012) (see next section). Moreover, activPAL3 has been considered to be the gold standard in measurement of sedentary behaviour in a recent study in healthy inactive individuals (18-65 year olds who walked < 5000 steps/day) (Ju'dice et al., 2015). Therefore, the activPAL3 monitor seems to be the most appropriate physical activity monitor use with in participants with medial knee OA in this work.

2.14. ActivPAL3 monitor

The activPAL3 monitor is a small activity monitor device worn throughout the day except during showering or swimming (not waterproof) on the mid-anterior aspect of the thigh using a PALstickie (double-sided hydro gel, hypoallergenic) (Ryan et al., 2006) (Figure 2-10). The device contains a triaxial accelerometer sensor which responds to the acceleration resulting from thigh movement. In addition, activPAL3 can monitor activity continuously for over seven days and summarise the collection data into 15 second epochs with activPAL3 software (Ryan et al., 2006; Aminian and Hinckson, 2012).

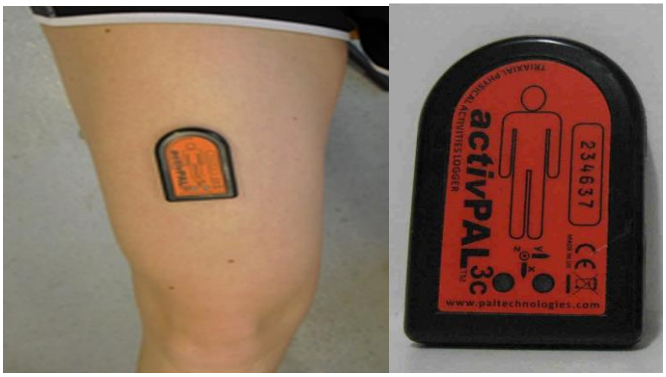


Figure 2-10: Location of the ActivPAL3 monitors, on the participants' thigh.

As a result of the activPAL's placement on the thigh, it is able to differentiate between upright positions (standing / walking) and sedentary behaviour; where this kind of data is not available with wrist, waist or ankle-worn accelerometers (Grant et al., 2008). The position and orientation of the activity monitor device could affect the accuracy of data captured particularly during walking. An activPAL3 is more accurate than waist- and ankle-mounted monitors for example: pedometers (walking) or Actigraph monitors (sedentary positions & walking) (Grant et al., 2008; Kozey-Keadle et al., 2011). In addition, there are no other movements that could alter or affect the data capture such as changes in pelvic alignment and movement (Grant et al., 2008). The potential reason for this is that activPAL3 is placed on the thigh to distinguish between changes in position and time spent sitting/lying, standing/stepping, and cadence (Dahlgren et al., 2010). The monitor uses the inclination of the thigh to classify posture. Therefore, the activPAL3 can distinguish upright postures (standing and stepping) and sedentary postures (sitting and lying). When the thigh is vertical it is classed as standing, and when an upright posture is detected the acceleration signal is further examined to detect cyclical stepping movements which are classed as stepping. Moreover, the posture is classified as sedentary (sitting and lying) when the thigh is horizontal (Grant et al., 2006). Also, it provides number of steps and cadence which can be used to calculate energy expenditure (Godfrey et al., 2008).

The activPAL3 monitor is suitable for use outside the laboratory because it is a small device and it collects the data at 20 Hz. In addition, ninety-two per cent of the older adult population (mean age 68 years) agreed to wear activPAL3 without any complaints because it is small, comfortable, does not restrict movement and does not show through clothing (Maddocks et al., 2010). Evidance has suggested that activPAL3 should be collected the data over 5 to 6 consecutive days for at least 6 hours a day to consider the data valid and accurate (Godfrey et al., 2007; Maddocks et al., 2010). Moreover, activPAL3 monitor not only measures time spent in upright position (standing/ walking), sedentary behaviour (sitting/lying), and number of steps in addition to cadence, but it also shows how long each walking period lasts and how many steps are taken during each walking period (Grant et al., 2008).

Ryan et al., (2006) investigated the validity and reliability of the activPAL3 monitor and pedometers (SW-200 and Omron HJ-109-E) in measuring walking (fast, normal, and slow) and cadence in adults with video observation. The participants included 12 women and 8 men aged 34.5 ±6.9 years. The subjects walked on a treadmill at different speeds from 0.9 m/s to 1.78 m/s and outdoors at slow speed, normal speed, and fast speed. They found that the correlation between activPAL3 and video

observation was excellent for all speeds for step count and cadence (ICC = 0.99), but the accuracy of the pedometer was affected by slow walking speed. Ryan et al., (2006) concluded that the activPAL3 monitor is a valid and reliable monitor to measure walking at all speeds and its accuracy is not affected by changes in walking speed.

Grant et al., (2008) evaluated the accuracy of activPAL3 in measuring number of steps and cadence in 21 older individuals (65-87 years old). They compared activPAL3 with two types of pedometers (NL-2000 and SW-200) in measuring steps and cadence on a treadmill at 5 different speeds (0.67, 0.90, 1.12, 1.33, and 1.56 m/s) and outdoors at 3 self-selected speeds (slow 1.37 m/s; normal 1.54 m/s; and fast 1.69 m/s) compared to direct observation. They found that activPAL3 was suitable and accurate for measuring cadence and step count on treadmills and out-doors especially at slow walking speed (0.90 m/s) with less than 1% error. However, the NL-2000 pedometer is more accurate than the SW-200 in measuring number of steps in older population. The two pedometers cannot measure cadence or detect changes in walking speed, particularly slow walking speed (percentage error was 23%) (Grant et al., 2008). The possible reason for this is that at a slow walking speed, the hip does not move enough to be detected by these pedometers. Another study was performed by Kozey-Keadle et al., (2011); the participants were inactive, overweight, and older people (aged 46.5±10.7). The researchers investigated the validity of activPAL3 and Actigraph for measuring sedentary behaviour compared to direct observation in older individuals in free-living environments. They found that activPAL3 and Actigraph underestimated sitting time by 2.8% and 4.9%, respectively. In addition, the correlation between activPAL3 and direct observation was r = 0.94, whereas the correlation between Actigraph and direct observation was 0.39. They concluded that only activPAL3 was able to detect reductions in sitting time. Thus, activPAL3 was more sensitive to reduction in sitting time and it is recommended to measure sedentary time in inactive, overweight, and older adults (Granat et al., 2007; Kozey-Keadle et al., 2011; Lyden et al., 2012).

Harrington et al., (2011) investigated the validity of activPAL3 and actigraph (GT1M) using a video recorded to measure walking at different speeds in 62 adult females' participant. They found no significant differences between activPAL3 and actigraph in measuring step number ($p > 0.05$); however, activPAL3 was more accurate and better than the actigraph in measuring steps at slow walking speed on a treadmill with the actigraph significantly underestimating the number of steps. The potential reason for this is that the actigraph is placed over hip and thereby the accuracy of this device to collect data may be influenced by pelvic movements (Grant et al., 2008).

The accuracy of activPAL3 was compared to direct observation in an investigation of 34 older individuals (range = 62-92.8 years old) (Taraldson et al., 2011). They measured sedentary behaviour (sitting and lying), transfer from sitting to standing, upright behaviour (standing and walking), and number of steps in three populations (acute stroke patients, older adults, and patients with hip fractures that had occurred 3 months earlier). Taraldson et al., (2011) found that activPAL3 was highly accurate in detecting and measuring sedentary behaviour and upright behaviour (100%) but less accurate in measuring the number of steps at a very slow walking speed (0.32 m/s). The potential explanation for this is that the walking patterns in stroke patients and patients with hip fractures are different form patterns in individuals with knee OA, as, during walking, they have very minimal hip and knee flexion and they may slide their affected limb with full knee extension during walking (Olney and Richards, 1996). Moreover, individuals with walking aids were recruited in this study, and therefore this procedure may influence the accuracy of the device for collecting the number of steps (Godfrey et al., 2007). They suggested that the activPAL3 should be attached to the unaffected limb. However, this suggestion cannot be generalised it to other populations.

Similar results were found by Aminian and Hinckson (2012); who examined the validity of activPAL3 for measuring sedentary behaviour and walking speed (fast, normal, and slow) in children. They measured sedentary time and walking speed in free-living activities followed by treadmill and over-ground activities. Aminian and Hinckson (2012) found that there was a strong correlation for time spent in sedentary positions, standing, and walking between the activPAL3 monitor and direct observation. In addition, the correlation between activPAL3 and video observation was high in measuring walking at different speeds. In addition, Lyden et al., (2012) found that activPAL3 was more valid for measuring the total sedentary time than actigraph (GT3X), when comparing the direct observation results (criterion measurement). The participants were healthy and between 20 and 60 years old. Under direct observation, activPAL3 accurately estimated sedentary time, and it was also sensitive enough to detect any reduction in sedentary time. Lyden et al., (2012) also found that actigraph was less accurate than activPAL3 in measuring the total sedentary time with significant differences in measuring the reduction of sedentary time under direct observation. They concluded that activPAL3 was a valid tool for measuring sedentary behaviour in free-living environments. Recently, the activPAL3 monitor has been used as a gold standard in a validation study comparing actigraph (GT3X) with the actiheart accelerometer in terms of accuracy for measuring sedentary behaviour (Ju'dice et al., 2015).

In summary, the activPAL3 monitor measures the amount of time spent sitting, lying, standing, stepping, and cadence. It is a suitable instrument to measure levels of physical activity in individuals with knee OA. The activPAL3 monitor is more valid for measuring sedentary behaviour of older populations than actigraph and it is better and more valid for measuring slow walking than the actigraph or pedometer. In addition, there was a strong correlation between activPAL3 and video observation of slow walking, time spent in sedentary position, standing, and walking. The activPAL3 monitor is more sensitive to reductions in sitting time than Actigraph and it is recommended for measuring sedentary time in inactive, overweight, and old adults (Granat et al., 2007; Kozey-Keadle et al, 2011; Lyden et al., 2012). Obese people walk slower than people weighting less (Mitsui et al., 2008) and potential have a similar walking pattern in knee OA. Therefore, the activPAL3 monitor is more accurate when measuring low intensity walking than a pedometer or actigraph.

Therefore, activPAL3 is suitable to use in this thesis to measure physical activity in individuals with knee OA and it can detect any change in sedentary behaviour, upright behaviour, and number of steps pre and post-intervention. In order to determine the most appropriate intervention that reduce loading and improve activity, the management approaches for knee OA will be explored.

2.15. Management of medial knee OA

Knee osteoarthritis causes reduced physical function (Suri et al., 2012) increased pain, reduced muscle strength and joint space narrowing, and thereby reduces the overall activity level (Salafi, 2005; Vincent et al., 2012). In addition, as a mechanical disease, the amount of load on the knee joint plays a vital role in progression of the disease as mentioned in the previous sections (Brandt et al., 2008). Although there is no known cure (Waller et al., 2013), a variety of treatment approaches attempt to reduce the load on the knee joint, limit the symptoms of knee osteoarthritis and delay or stop disease progression such as surgical interventions, pharmacological, and non-pharmacological treatment.

2.15.1. Surgical management of medial knee OA

Surgical realignment intervention, such as total knee replacement (TKR), unicompartmental knee replacement (UKR), or the high tibial osteotomy (HTO), aims to relieve and reduce the load on the knee joint when non-surgical intervention fails (Andriacchi, 1990; Wada et al., 1998).

TKR has been used when there is severe damage in the tissues causing severe pain and severe functional limitation during walking and physical activity (Mancuso et al., 1996) and it is the definitive procedure for management of knee OA. However, good to excellent results can be achieved by TKR, some functional limitations are still there and some individuals may not be suitable for this kind of surgery (≤ 65 years-old) (Andriaccchi, 1982; Callahan et al., 1994).

HTO and UKR are commonly recommended for younger individuals (≤ 60 years-old) who have unicompartmental arthritis because the results of these surgical procedures are worse in elderly adult patients (≥ 60 years old) compared to younger adult patients (Insall et al., 1984).

Uincompartmental Knee Replacement (UKR) is considered as the right option before the TKR for medial compartment knee OA when the soft tissues are severely damaged. The UKR is used to preserve the soft tissues in the unaffected side and thereby maintain the normal knee function and proprioception compared to TKR (Lonner, 2009)

High tibial osteotomy (HTO) is a surgical intervention used to reduce the load on the knee joint and postpone total joint replacement by removing a part of bone on the proximal tibia to unload the medial compartment of the knee (Wada et al., 1998). This procedure leads to a redistribution of the load on the medial compartment of the knee joint. Thus, the EKAM is reduced by approximately 30 to 50 % (Prodromos et al., 1985); however, the adduction moment tends to increase gradually over

one to five years after high tibial osteotomy (Wada et al., 1998; Grelsamer, 1995; Miyazaki et al., 2002) leading to a TKR.

Given the risk associated with knee surgery and the time in rehabilitation and potentially restricted function, there are many individuals who may want the surgery. Additionally, there will be many individuals who are not suitable for surgery due to their age or general health, and therefore other interventions may be used to reduce their knee pain, improve function, and help to decrease the load on the knee joint. There are grouped into pharmacological, exercise regimens and orthotic management.

2.15.2. Pharmacological treatment of medial knee OA

Pharmacology modalities such as anti-inflammatory drugs and/or paracetamol reduce knee pain and relieve symptoms; however, loading on the knee joint is still there and tends to increase over the time (Schnizer et al., 1993; Huskinsson et al., 1995). Therefore, pain relief by pharmacology modalities has been associated with an increased the load on the knee joint over the time (Sum et al., 1997; Hurwitz et al., 2000).

Huskinsson et al., (1995) found that non-steroidal anti-inflammatory drugs (NSAIDs) had significant effect on pain with knee OA while the EKAM was increased over the time leading to surgical intervention. Therefore, reduction knee pain in individuals with knee OA may encourage them doing high level of physical activity. However, the loading on the knee joint still there and may be increased during physical activity (Wideman et al., 2014). Lena et al., (2010) found that tanezumab drug (common uses to reduce knee pain in osteoarthritis) reduced knee pain during walking by 45-62% from baseline; however, individuals with knee OA were going to a knee replacement too early (Lane et al., 2010). The knee loading (EKAM) is increased when taking analgesics and non-steroidal anti-inflammatory drugs and thereby disease progression was found to be developed over time (Schnitzer et al., 1993; Huskisson et al., 1995); however, NSAIDs have a significant effect on pain with in individuals with knee OA. This may be explained by a high level of physical of activity is associated with 1.35 times greater risk of cartilage lesion (Kumar et al., 2014). Therefore, the load on the knee joint (EKAM) and knee cumulative loading in individuals with medial knee OA are most important with treat medial knee OA.

2.15.3. Conservative management approaches

The conservative interventions recommended by the UK national guidelines for their safety and effectiveness in pain relief and improve function (National Institute for Health and Clinical Excellence (NICE), 2008) There are a plethora of conservative management approaches in the literature include exercises, education, weight loss if overweight or obese, hot and cold packs, and orthotics. Nevertheless, these are expensive interventions that require regular revising depending on the patient's age and level of physical activity (Griffin et al., 2011).

This review here will focus on two of the most common: strength exercises and orthotic management.

2.15.3.1. Exercise

Exercises are recommended as a core intervention for people with knee osteoarthritis to reduce pain and improve function (Zhang et al., 2008), but they do not reduce the EKAM, and thereby may increase disease progression (Andriacchi, 1994; Bennel et al., 2010; Hinman al., 2013). An observational study found that stronger quadriceps were not associated with reduced progression of knee OA when the muscle strength was assessed by isokinetic dynamometry at baseline and 2.5 years later for 79 subjects with knee OA (Brandt et al., 1999). Moreover, stronger quadriceps muscles were correlated with higher progression of knee OA in individuals with medial knee OA (Sharma et al., 2003a). Chang et al., (2005) observed that there was a correlation between hip abductor muscle weakness at baseline during walking and the progression of knee OA over 18 months. They suggested that strengthening hip abductor muscles may reduce the load on the knee joint in individuals with knee OA. However, this correlation between muscles strengthening and knee loading (the EKAM) does not find in any recent studies (Bennell et al., 2010; Foroughi et al., 2011; Ferreira et al., 2015).

In a randomised control trial (RCT) of a 6-month high intensity progressive resistance training programme found that the first peak knee moment in the frontal plane did not reduced (Foroughi et al., 2011) in individuals with medial knee OA whereas, pain and function were improved by strengthening hip and knee muscles. EKAM reduction was not observed after 12-week home exercise programme (Bennell et al., 2010), 6-week strengthening exercise programme (Al-Khlaifat et al., 2015), and no correlation was found at baseline (Kean et al., 2015).

An intervention study was performed by Bennell et al., (2010) with 89 individuals with medial tibiofemoral OA. They were divided into a 12-week home exercise programme group and a no intervention control group. They found that knee pain, physical function, and muscle strength were

improved significantly in the intervention group at 12 weeks comparison with the control group. However, the EKAM was increased in the exercise group over 12 weeks (Bennell et al., 2010). In a recent study, the authors investigated the relationship between hip abductor muscle strength and EKAM in 99 subjects with mild to moderate medial knee OA (Kean et al., 2015). They found that there was no correlation between the EKAM and hip abductor muscle strength at baseline ($r=0.04$, $p >0.05$).

In a recent systematic review that investigated the effect of exercise on EKAM in individuals with medial tibiofemoral OA (Ferreira et al., 2015), it was found that knee pain and physical function significantly improved in the exercise groups compared to the control groups (sham groups); however, no significant differences have been shown between strengthening and control groups regards the EKAM reduction. They concluded that an exercise intervention may not protect individuals with medial knee OA from joint loading. Therefore, reducing the knee pain with exercises in individuals with medial knee OA whilst the EKAM is still high, may increase disease progression over the time. However, the physical activity may be improved by exercise but the adherence of the individuals to exercise continuation is poor (Pisters et al., 2007) and exercises unfortunately have no effect on knee loading.

As medial knee OA is a mechanical disease, GRF displacement more medially to the centre of knee joint, biomechanical intervention is needed to alter the GRF line alongside pain score.

As medial knee OA is a mechanical disease, altering the joint to be closer to the GRF or altering the vector to be closer to the knee joint are appropriate methods to reduce knee loading.

2.15.3.2. Conservative orthotic management

Valgus knee braces and lateral-wedge insoles are common methods used to alter the GRF line directly and indirectly, respectively, and to thereby diminish the load on the knee joint and reduce the symptoms in individuals with medial knee OA. Valgus knee braces are used to decrease the load on the medial tibiofemoral joint by correcting the varus knee alignment in individuals with medial knee OA (Horlick and Loomer, 1993) by applying three-point forces to their affected knee (Pollo et al., 2002). As depicted in Figure 2-11, force F1 is being applied by the force strap, while forces F2 and F3 are being applied on the thigh and leg in a lateral direction to decrease the medial compartment load (Pollo et al., 2002). This gives the intervention a direct application encompassing the knee joint.

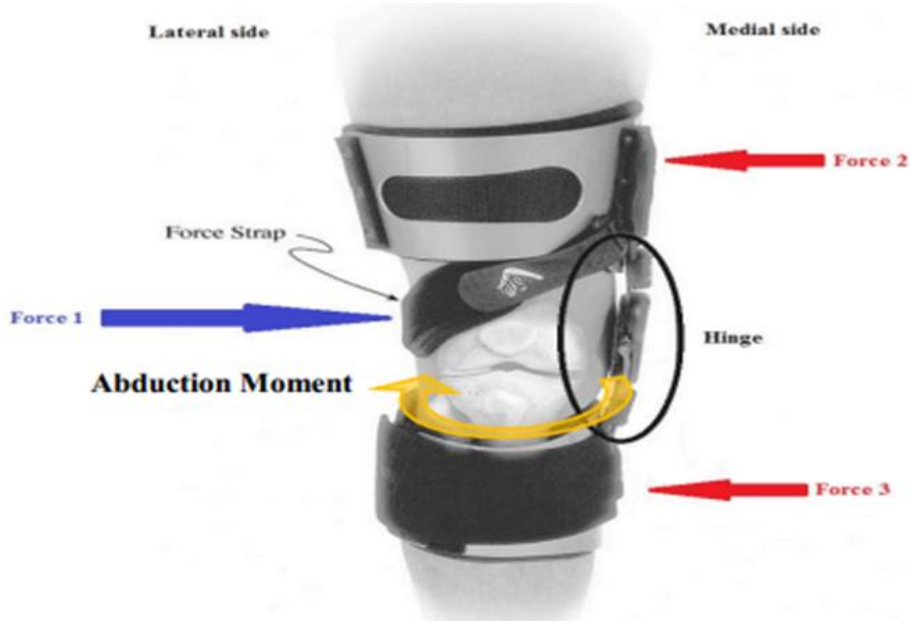


Figure 2-11: Valgus knee brace with three-point forces. Force (1) represents medial directed force applied by force strap, forces (2) & (3) represent lateral force applied on thigh and led (Pollo et al., 2002).

Valgus knee braces have a significant positional effect on symptoms, as knee stability, knee pain, physical function and walking speed were improved in individuals with medial knee OA (Hewett et al., 1998; Pollo et al., 2002; Ingvarsson et al., 2010; Jones et al., 2013a).The EKAM was significantly reduced with valgus knee braces by 11% (Pollo et al., 2002) and 7% (Jones et al., 2013a) and thereby disease progression was delay (Miyazaki et al., 2002). However, Hewett et al. (1998) did not find any reduction in EKAM in individuals with medial compartment OA when using knee braces. This may be explained by the use of different designs of knee braces in the studies and the adherence among patients to wearing the knee braces.

While valgus knee braces improved pain (Van Raaij et al., 2010), function, and decreased knee loading in individuals with medial knee osteoarthritis (Fantini-Pagani et al., 2012), they are expensive and some individuals may refuse to wear braces once prescribed (Squyer et al., 2013). They may also cause skin sensitivity, and reduce knee flexion during walking in individuals with medial knee OA (Kirkley et al., 1999; Richards et al., 2005). Jones et al., (2013a) compared the biomechanical and clinical effects of valgus knee brace and lateral wedged insole in individuals with medial knee OA. They found that there were no significant differences between these two interventions in pain and function improvement; however, the lateral wedged insoles showed greater levels of acceptance by patients. In addition, lateral wedged insoles significantly reduced the first peak of EKAM and KAAI compared to knee brace (Jones et al., 2013a). Therefore, they are discussed in the following sections.

2.15.3.3. Lateral Wedge Insole

Lateral-wedge insoles (LWIs) are a simple conservative approach in treating medial compartment knee OA. In comparison with valgus knee braces, there are an indirect orthotic intervention, low-cost, simple to use intervention that, were first reported by Sasaki and Yasuda in 1986. A lateral wedged insole (Figure 2-12) is an insert for shoes, whose the lateral border is thicker than medial border to shift the centre of pressure (COP) and the line of the ground reaction force (GRF) more laterally to the knee joint by altering the angle of the calcaneus into a valgus position (Pollo, 1998). Therefore, as the moment arm decreases, this result in a reduced load on the knee joint in individuals with medial compartment OA of the knee joint (Kerrigan et al., 2002; Kakihana et al., 2005).

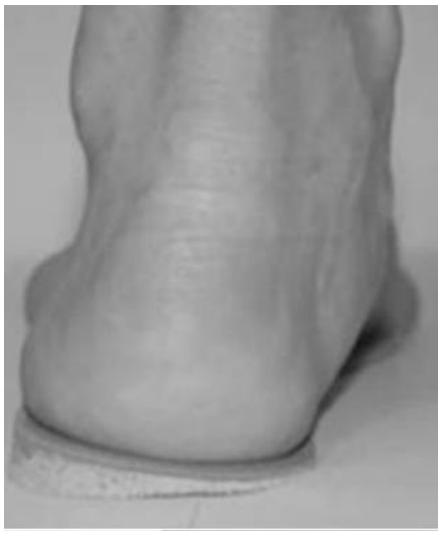
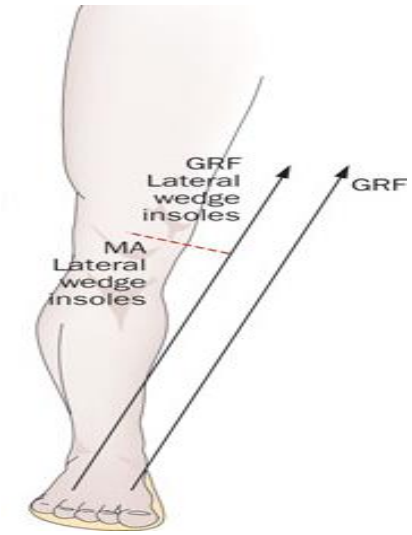
A  B 

Figure 2-12: (A) Typical LWI (posterior view), (B) Effect of LWI on GRF line & moment arm (anterior view) (Reeves & Bowling, 2011).

The calcaneus angle plays a critical role in the kinetics of the knee joint. Therefore, by everting the foot when using lateral wedged insoles by altering the angle of calcaneus into valgus position (Pollo et al., 1998), the knee joint is moved laterally towards the centre of the body, moment arm reduced and thereby the EKAM is decreased and thereby varus knee alignment is reduced (Sasaki and Yasuda, 1987). Therefore, lateral wedged insoles are recommended by the National Collaborating Centre for Chronic Conditions (2008) and by 13 out of 14 international guidelines for the management of knee OA, American Academy of Orthopaedic Surgeons (AAOS) not recommended LWIs, 2008, (Jorden et al., 2003; Zhang et al., 2010). Using lateral-wedge insoles is considered a

conservative (non-pharmacological) intervention in individuals with knee OA (Jordan et al., 2003; Bennell and Hinman, 2005; Zhang et al., 2010) to potentially reduce symptom exacerbation and disease progression by altering the GRF and decrease the load on the knee joint (NICE, 2008). In order to fully understanding the role of lateral-wedge insoles in medial knee OA, the biomechanical and clinical effects will be presented in the next sections.

2.15.3.3.1. Biomechanical effects:

Lateral wedged insoles were compared with medial wedged insoles in the first gait analysis study performed by Ogata et al (1997) in 40 healthy participants (control group; no insoles) and 50 individuals with medial knee OA (treatment group; lateral and medial wedged insoles). They used a uni-axial accelerometer to investigate the lateral and medial thrust at the knee joint during early stance. They found that the load on the medial compartment was reduced by using lateral wedged insoles, whereas, it was increased by using medial wedged insoles. However, the biomechanical effects of insoles on knee thrust were investigated in Ogata et al., (1997) study, not the kinetic variables (e.g. EKAM). Ogata et al (1997) recommended lateral wedged insoles for patients with painful medial compartment OA, as the lateral wedged insoles have been used to reduce medial thrust. Crenshaw et al., (2000) was the first study that investigated the effect of lateral wedged insoles on kinetics at the knee joint (e.g. EKAM) in 17 healthy participants. They measured temporal, spatial, angles, and forces variables at hip, knee, ankle with and without 5° lateral wedged insoles using three-dimensional gait analysis. There were no significant differences in any variables; however, the EKAM significantly reduced in 14 participants by an average of 7.3%.

The biomechanical effect of lateral wedged insoles on the EKAM was investigated and compared to a shoe without an insole and a shoe with a neutral insole (flat insoles) (Kerrigan et al., 2002). The first peak EKAM during early stance was significantly reduced by 5.3% in the 5° lateral wedged insole group compared to the no insole group of individuals with medial knee OA. Moreover, there was a significant reduction in the first peak EKAM (3.8%) in 5° lateral wedged insoles compared with neutral insoles (Kerrigan et al., 2002). The 2nd peak EKAM was significantly decreased in the group using lateral wedged insoles compared to the other groups (no insole and neutral insoles). Therefore, the results showed that the EKAM was reduced during walking in the lateral-wedge insole group compared to the walking with no insoles and walking with non-wedged insoles groups. The results suggested that lateral wedged insoles are biomechanically effective and reduce loading on the medial compartment in medial knee osteoarthritis patients. Hinman et al., (2008) results support these results in a matched population.

The immediate effect of lateral wedged insoles were investigated in an RCT study (Hinman et al., 2008). Forty participants wore their usual shoes with and without lateral wedged insoles (5-degree inclination, made of high density ethylene-vinyl acetate) in random order to investigate the immediate effect of lateral wedged insoles in individuals with medial knee OA (Hinman et al., 2008). The first peak EKAM was reduced by 0.22 Nm/Bw.Ht% with an improvement in walking pain of roughly 24% when participants wore their shoes with lateral wedged insoles (Hinman et al., 2008). A similar effect was found in 28 patients with knee OA after they wore standardised shoe with 5-degree lateral wedged insoles over two weeks compared to baseline (same footwear with flat insoles) in a crossover study (Jones et al., 2013a). The EKAM and KAAI were significantly reduced when using the lateral wedged insoles by 12% and 16.15 compared to baseline, respectively.

Moreover, in the first study which evaluated whether the effect of lateral wedged insoles declined over one month in 20 individuals with medial knee OA (Hinman et al., 2009). The 1st and 2nd peaks of the adduction moment, as well as the KAAI, were reduced similarly significantly at baseline (immediate effect) and after a 1-month follow-up using a 5° lateral-wedge insole for an average of 8 hours a day compared to the control group (no insoles) (Hinman et al., 2009). Additionally, they found that the higher users of the LWIs demonstrated similar reductions in the EKAM and KAAI as subjects who were low users. They concluded that the immediate beneficial effects of the lateral wedge insole on the EKAM remained even after the insole had been worn for one month and that the EKAM did not decline over one month (Hinman et al., 2009).

In addition, the effect of lateral-wedge insoles on knee loading was investigated over 12 months and compared to neutral insoles (comparator insoles) (Barrios et al., 2013). Nineteen participants were assigned to each group (lateral wedged insoles and neutral insoles) and assessed at baseline and after 12 months via three-dimensions. The groups were not significantly different for age and radiographic disease severity at baseline. Barrios et al., (2013) found that the EKAM and KAAI were significantly decreased using lateral-wedge insoles (high density-70 durometer) over 12 months on two visits (baseline and one month later) and compared to neutral insoles. Therefore, there was a significant difference between both sessions of the lateral wedged insole group and this differences was observed between both groups over 12 months which means that the lateral wedged insoles have a significant effect on the EKAM.

It has been identified from the findings of the large cohort study conducted by Hinman et al., (2012) that 5˚ lateral wedges (57.5 Shore A hardness) immediately decreased the peak knee adduction moment and knee adduction angular impulse where the knee ground reaction force lever arm decreased with 5-degree lateral wedges. The findings of the research study explained that lateral

wedges decreased peak knee adduction moment and knee adduction angular impulse by 5.8% and 6.3%, respectively, in individuals with knee OA. The centre of pressure was displaced more laterally when using lateral wedged insoles and thereby the length of the moment arm (knee ground reaction force lever arm) was reduced, and thereby reducing the EKAM (Hinman et al., 2012). The effectiveness of lateral wedged insoles on the EKAM in individuals with medial knee OA has been confirmed in a recent systematic review (Radzimski et al., 2012) which recommended high-density insoles, and it was observed in the majority of the studies that they maintain their effectiveness over time (Hinman et al., 2008, 2009 & 2012; Jones et al., 2013a & 2014). A recent systematic review stated that custom-made insoles with high density ethyl vinyl acetate (57.5-70 shore type A) is an effective and recommended to maintain effectiveness of lateral wedged insoles over the time where the high density (e.g. > 55 durometers) represent a high resistance to compressive deformation (Radzimski et al., 2012). Additionally, a recent review performed by Hinman (2013) concluded that the EKAM which is a surrogate measure of medial compartment load is reduced significantly by wearing lateral wedged insoles in individuals with medial knee OA. A recent meta-analysis performed by Arnold et al (2016) found that the LWI resulted in a small but statistically significant reduction in the 1st peak and 2nd of the EKAM with ineffective on disease progression in individuals with medial knee OA. This may be explained by the reduction in knee loading was small and thereby it has supposed that a larger reduction in knee loading may be reflected on structural changes and delay disease progression. However, evidence has shown that the risk of progression of knee OA increased 6.46 times when the first peak of EKAM increases by 1% (Miyazaki et al., 2002) and thereby any reduction in knee loading may have beneficial effect on disease progression. The other potential reasons this may LWI does not effective on progression of knee OA is that. The other potential reasons is that the effectiveness of LWI on disease progression may be diminished by other factor such as changing in level of physical activity where a high physical activity (stepping >10,000 steps/day) not recommended for individuals with knee OA and associated with 1.35 times greater risk of disease progression (Dore et al., 2013; Lin et al., 2013). However, no previous studies have been undertaken before on level of activity in medial knee OA with the LWI intervention.

A recent study by Jones et al., (2014) found that a 5-degree lateral wedged insole with medial support significantly reduced the EKAM and KAAI by 6.29% and 5.55%, respectively, compared to baseline (control shoes) in individuals with medial knee OA and that there were no significant differences between treatments groups (5-degree lateral wedged insoles with and without medial support). However, the difference between LWIs (with and without support) in term of EKAM reduction was 1.08% for lateral wedged insoles with medial support (Jones et al., 2014) alongside it was

comfortable for the users. The reduction of the EKAM was diminished by 1% over six months when wearing the lateral wedged insole without medial support may be because it was not comfortable (Duivenvoorden et al., 2014). They found that there was no significant difference in the maximum knee flexion moment (KFM) between control shoe and LWIs, even it increased in medial supported lateral wedged (biomechanical responders) group by 2.73%.

Different inclination of lateral wedged insoles

The amount of wedging of lateral wedged insoles is one of the potential reasons for the variation in the magnitude of EKAM reduction among the existing studies. However, a higher wedge offers greater reduction, but it causes greater discomfort for the users (Kerrigan et al., 2002; Butler et al., 2007; Radzimski et al., 2012). This discomfort could diminish the effect of lateral wedged insoles in clinical findings as Jones et al., (2014) conclude that discomfort for long term when using lateral wedged insoles may result in knee pain. Additionally, greater care should be taken to prevent subtalar joint injuries by excessively increasing movement and joint moment (eversion) at the rear-foot (Butler et al., 2007), and therefore the amount of wedging plays a critical role when choosing lateral wedge insoles in this thesis. According to a 1% increase in the EKAM on the 1st peak EKAM has been shown to be associated with a 6.46 times higher risk of knee OA progression (Miyazaki et al., 2002) and a 1mm laterally displacement of the line of GRF decreases the EKAM by 2% on the 1st peak EKAM (Shelburne et al., 2008). Thus, any reduction in the EKAM is considered significant. Kerrigan et al., (2002) have evaluated the effect of lateral-wedge insoles inclined at 5° or 10° compared to no insoles and wearing non-wedged insoles on EKAM in individuals with medial knee OA. The results suggested that both lateral wedged insoles were biomechanically effective at reducing the EKAM in individuals with medial knee OA; however, the 5° wedge was more comfortable than the 10° wedge to wear inside one's own shoes. They demonstrated that the EKAM significantly reduced by 6% by wear the 5˚ lateral-wedge insole (Kerrigan et al., 2002).

Butler et al., (2007) compared different degrees of wedging, ranging from 5˚-15˚, regards comfort in individuals with medial knee OA, and they showed that higher wedging caused more discomfort for users. A 5-degree wedge was recommended for individuals with medial knee OA in terms of comfort compared with higher wedging, whereas the difference between 3.5 and 5-degree wedge was quite small and no users reported any issues with 5-degree (Kakihana et al., 2004; Radzimski et al., 2012; Hatef et al., 2014). Thus, a 5-degree wedge offered a greater reduction in the EKAM and when considering comfort score, the 5-degree lateral wedged insoles offered the best solution for medial knee OA.

2.15.3.3.2. Clinical effects

The effect of lateral wedged insoles on clinical outcomes (pain and analgesic intake) was first investigated in individuals with medial knee OA (Sasaki and Yasuda., 1987). Knee pain and walking ability were improved in individuals with medial knee OA using a combination of lateral-wedge insoles with NSAIDs (Indomethacin, 600 mg/day) in comparison with patients who only used NSAID treatment over one to five years with mild to moderate knee OA (Sasaki and Yasuda, 1987). Knee pain did not improve in the NSAIDs group because the EKAM may increase over the years (Miyazaki et al., 2002). Mailefert et al., (2001), in a prospective study conducted over six months, investigated the effect of lateral wedged insole and neutral insoles relation to NSAID intake in individuals with medial knee OA. The medication intake was reduced in the lateral wedged insole group compared with the control group (neutral insoles) over six months. Moreover, NSAID intake was measured by Pham et al., (2004), in prospective study over two years. It compared a lateral wedge insoles group with a neutral insoles group (control group) in individuals with medial knee OA. They reported that the number of days with NSAID intake was reduced in the lateral wedged insoles group. Therefore, those results confirmed that LWIs have reduced the NSAIDs intake compared to control groups (no intervention and neutral insoles). Additionally, individuals with knee OA use NSAIDs to relieve knee pain and a reduction in NSAIDs intake potentially result of a reduction in knee pain. Pham et al (2004) also found that there was no statistically significant difference between the two groups regarding pain improvement; however, the compliance was satisfactory (85.8% for LWI group) over two years. One potential reason that pain reduction did not occur is that the effectiveness of LWIs may be decreased over the years because of loss of density, and thus the clinical effect of LWI may be diminished (Radzimski et al., 2012). Therefore, LWIs with high density (55 and 70-durometer density foams) have been shown effective over time and are used in the majority of studies (Kerrigan et al., 2002; Bennell et al., 2011b; Jones et al., 2013a).

In a more recent study, Baker et al., (2007) conducted a crossover trial, detecting a small effect of lateral-wedge insoles on pain with medial knee OA patients. Eighty-six participants were randomised to receive a 5˚ lateral-wedge insole or a neutral insole for 6 weeks (average 7 hours/day) following a 4-week washout period. They concluded that there was no obvious clinical or statistical significance between the groups regarding pain and NSAIDs intake; however, the pain improved in the lateral wedge insole group compared to the neutral group (difference was 13.8). One potential reason that pain and NSAIDs did not significantly changed in LWI`s group is that the LWIs worn in the affected side only, whereas the neutral insoles were worn on the contralateral side in treatment group. Therefore, this asymmetry may effect on the clinical outcomes. The other potential

confounding factor is that there was no significant improvement in knee pain compared to the neutral insole because the individuals may experience a placebo effect from the neutral comparator insoles (Parkes et al., 2013). Parkes et al., (2013), in a recent meta-analysis, noticed that in 12 trials where the control group used a neutral insole, the lateral-wedge insole showed no association with a reduced WOMAC pain score. Therefore, they concluded that a lateral-wedge insole does not reduce pain more effectively than a neutral insole. One of the potential reasons for this is that the individual would receive a placebo effect from the comparator insole, which would be reflected in their pain response.

Lateral-wedge insoles immediately improve knee pain and physical function in individuals with medial knee OA after three months compared with their own shoes (with no insoles) (Hinmain et al., 2008). The knee pain and function improved by 22% and 20%, respectively, in participants with medial knee OA after wearing lateral wedged insoles for 3 months. They were assessed at baseline and three months later by Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (Hinman et al., 2008). The effectiveness of 5° lateral wedged insoles and neutral insoles was investigated in individuals with medial knee OA over one month and at a one-year follow-up (Barrios et al., 2009b). They found that WOMAC pain and function subscales improved significantly in both groups (lateral wedged insoles group and neutral insoles group) at a one month and a one-year follow-up compared to baseline and they had the same clinical effect. However, there was no significant difference between results at the one month and the one-year follow-up in a between groups comparison. This could be explained by the fact that individuals would receive a placebo effect from neutral insoles (control group). However, the EKAM was not measured by Barrios et al (2009b), but it was found to be increased (KAAI as well) with neutral insoles compared to 5-degree lateral wedged insoles over one year in individuals with medial knee OA in another study (Barrios et al., 2013). Therefore, it is possible that cumulative knee loading may be increased in the lateral wedged insoles group, resulting in an improvement in physical activity (stepped more steps), and therefore knee pain was observed over one year in a lateral wedged insoles group. Similarly, there were no significant differences in WOMAC pain and function subscales over 12 months when using 5-degree lateral-wedge insoles (intervention group) compared with neutral insoles (control group) (Bennell et al., 2011b). Moreover, Bennell and her colleagues (2011b) showed a small mean reduction in WOMAC pain and function subscales when comparing between groups. However, these reductions were smaller and made a minimally clinical important difference. This small difference may be explained by that the knee pain and function were assessed only twice with a long period between them (at baseline and after 12 months).

Importantly, the number of steps was measured in Bennell et al.,'s (2011b) study in both groups during baseline and over 12 months using pedometers (Omron HJ-005, worn at the waist) as a secondary outcome measurement. They stated that the number of steps did not significantly increase over 12 months compared with baselines and between groups; however, the number of steps decreased in the neutral group by -874 steps/day (11.5%). This decrease in the number of steps in the neutral group could be due to knee pain because the level of activity is affected by the presence of knee pain in individuals with knee OA (Van Damme et al., 2004; Goubert et al., 2004; Cavanaugh et al., 2007; Rakel et al., 2012; Wideman et al., 2014). In contrast, as shown in Table 2-3, the number of steps was increased by + 151 steps/day (1.9%) with a minimal mean reduction in knee pain when 5-degree lateral wedged insoles were used. There are many potential explanations for minimal reduction of knee pain. Firstly, the EKAM was not measured in their study, therefore it is not known whether LWI had a biomechanical effect which are supposed to reflect on clinical findings. The other potential reasons is that the EKAM was reduced by wearing 5° lateral wedged insoles (was not measured in this study) and as result of that the knee pain decreased significantly at any time point, between baseline and before the second assessment, and thereby the number of steps increased significantly as well. Therefore, the individuals with medial knee OA would walk to their pain threshold and the levels of pain went up before the second assessment. The third potential explanation is that the LWI was effective on knee pain throughout the intervention but because of the changing in the amount of the knee loading during activity, the effect of LWI on knee pain was diminished. Additionally, presence of back pain and foot pain, which appeared in a low percentage of the 5-degree lateral wedged group, may not be directly due to wearing 5˚ lateral wedged insole, but it could be additional proof for improvement in physical activity and discomfort insoles. Also, Bennell et al., (2011b) used 5˚ lateral wedged insoles made from ethyl-vinyl acetate, the high density of these insoles (similar to a running shoe), which were uncomfortable for users. Jones et al., (2014) found that comfort score and pain rating were strongly correlated, therefore pain response may be affected by the comfort of the insoles. Finally, the adherence of the individuals to wearing the pedometer may have been low, and thus some of the activity levels may not have been recorded.

Table 2-3: Difference in pain, function, and number of daily steps within and between groups from baseline to 12 months follow-up (Bennell et al., 2011b).

	Baseline (Week-0)		Month-12		Within group (Diff)	
outcomes	LWI	Neutral	LWI	Neutral	LWI	Neutral
Pain (0-10)	4.0	4.3	3.1	3.1	0.9	1.3
WOMAC-pain (0-20)	7.1	7.2	6.4	6.2	0.7	1.2
WOMAC-function (0-68)	23.7	23.6	20.8	20.1	3.1	4.0
Steps/day	7908	7562	8059	6688	+151 (1.9%)	-874 (11.5%)

Knee pain and NSAID intake were investigated in individuals with medial knee OA by using 5° lateral wedged insole (made of ethyl-vinyl acetate) (Hatef et al., 2014). They concluded that a 5° lateral wedged insole was more effective for pain than a neutral insole; the mean differences were 29.3% and 6.25% for LWI and neutral insole, respectively, compared to baseline (within group); however, the pain was significantly reduced in both groups over 2 months compared to baseline. Additionally, the number of NSAIDs taken was reduced significantly in the group with 5˚ lateral wedged insoles compared with baseline, but this reduction was not shown when neutral insoles were used over 2 months. This reduction in the number of NSAIDs taken may indicate a reduction in knee pain because of lateral wedged insoles. The results of Hatef et al (2014) showed the differences within groups at baseline and 2-month follow-up for each group, but the differences between groups were not calculated in this study.

To conclude this section, the EKAM reduction occurs immediately and after a period in individuals with medial knee OA when using lateral wedged insoles. Moreover, evidence has demonstrated that lateral wedged insoles with a 5-degree inclination with medial support and with > 55 shore A hardness (especially 70 Shore A hardness) offer a greater EKAM reduction with more comfort for the users and maintain their effectiveness in the long-term, and therefore offer the best treatment for medial knee OA. Knee pain and functional improvement were also found when using lateral wedged insoles in comparison with baseline (Barrios et al., 2009b; Jones et al., 2013a) and control groups (no insole) (Hinman et al., 2008), but recent randomised trials have failed to find that reduction in comparison with a neutral insole (Baker et al., 2007; Bennell et al., 2011; Parkers et al., 2013). Jones and his colleagues (2014) investigated the relationship between responders (decreased EKAM) and non-responders (increased EKAM) and knee pain (using KOOS pain subscale) in 70 patients with medial knee OA. They concluded that there is no obvious relationship between change in knee medial loading when wearing LWIs and corresponding change in knee pain. However, knee pain

reduction was significant in medially supported lateral wedged insole compared to control shoe (Ecco Zen) ($p<0.001$).

Thus, 5˚ lateral wedged insoles offered a significant EKAM reduction, greater comfort for users and may have diminish clinical effect with considering cumulative knee loading during physical activity in knee OA. Therefore, the pain reduction may not have been observed because overall activity changed and individuals walked to their respective pain level.

2.16. Gaps in literature

In reviewing the literature, the external knee adduction moment has been shown to be an objective measure for progression of medial knee osteoarthritis (Miyazaki et al., 2002). Conservative treatments are designed to reduce this EKAM which ultimately would aim to have a clinical effect as well as a biomechanical effect. Evidence has shown that the external knee adduction moment is reduced significantly when using lateral-wedge insoles (Jones et al., 2012; Jones et al., 2013), however, pain and physical function do not improve significantly (Radzimski et al., 2012; Parkes et al., 2013; Hinman et al., 2013). One of the potential reasons this may not occur is that an activity profile has changed and they walk to their respective pain level. The other confounding factor in studies investigating pain is that the individual would receive a placebo effect from the comparator insole and therefore objective measures are needed in addition to simple subjective pain measures. It is therefore not known if a change in the activity level of the individual is seen with lateral wedge insoles which may counteract the reduction in symptoms that the individual is experiencing when on treatment.

Furthermore, the results of such a trial should have a combined output which targets both the clinical (pain, activity) and biomechanical. This would then determine whether LWIs are an the most efficacious treatment of medial knee OA. Additionally, evidence has shown that physical activity may correlate and affected by knee pain score. Moreover, a high physical activity (doing> 10.000 steps/day) is not recommended in individuals with knee OA because this level of activity was correlated with cartilage loss.

In conclusion, to our knowledge, no study has investigated the effect of lateral wedge insoles on activity level using an activity monitor. Moreover, no study has investigated the effect of LWIs on osteoarthritis pain, level of physical of activity, and knee loading in one study. Cumulative knee loading which considers the level of physical activity will be investigated in individuals with knee OA to determine any change that may occur after one and six week use of LWIs and whether the cumulative knee loading increased alongside physical activity. Therefore, this study will be the first study to investigate in cumulative knee load after LWIs intervention.

In order to fulfil these gaps in literature we plan to perform a trial whereby individuals with medial knee OA will wear a lateral wedged insoles for a period of six weeks repeated activPAL3 monitor collections (for three separate weeks).

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2.16.1. Objectives of the PhD

The following will help us to understand the effect of lateral wedged insole on knee loading, level of physical activity, and knee pain. Secondly, they will allow us to determine if lateral wedged insoles are an efficient intervention for patients with medial knee OA.

2.16.2. Aims and Hypotheses

The primary aims are to determine whether a lateral wedged insole improves physical activity in individuals with medial knee OA and whether this improvement concurrent with reductions of the knee loading. Five hypotheses will be tested in this thesis:

1. To determine any reduction in knee load with using lateral wedged insole in comparison to the comparator group.

- Null hypothesis, There will be no significant reduction in the external knee adduction moment in the group using the lateral wedged insole compared to the comparator group.

2. To determine if there is any change in activity level due to using the lateral wedged insole compared to the comparator group.

- Null hypothesis, There will be no significant difference in level of physical activity in the group using the lateral wedged insole compared to the comparator group.

3. To determine any change in pain and function after wearing lateral wedged insole in comparison to the comparator group.

- Null hypothesis, There will be no significant difference in knee pain and function in the group using the lateral wedged insole compared to the comparator group.

4. To determine any change in cumulative knee loading lead in the group using the lateral wedged insole compared to the comparator group.

- Null hypothesis, There will be no significant difference in cumulative knee loading in the group using the lateral wedged insole compared to the comparator group.

5. To determine any improvement in dynamic balance after using lateral wedged insole in comparison to the comparator group.

- Null hypothesis, There will be no significant difference in dynamic balance in the group using the lateral wedged insole compared to the comparator group.

Moreover, this study will help to identify whether the physical activity will be recommended to measure objectively as a primary measurement alongside knee pain in knee OA research studies.

However, before any study can be embarked upon, the repeatability of the methods that will be used in the study will be undertaken in the next chapter

Chapter Three

Test-retest repeatability of gait, and dynamic balance data

3.1. Introduction

This thesis aimed to investigate the effect of lateral wedged insoles on physical activity, pain, gait kinetics and kinematics, and dynamic balance in individuals with medial compartment OA of the knee joint at baseline, one week, and six weeks, respectively. Moreover, it investigated the effect on knee pain, physical function, and quality of life (self-report questionnaires).

Therefore, the aim of this chapter is to assess the test-retest repeatability of the gait kinetics and kinematics, and dynamic balance in medial knee OA patients between days. This will ensure that the differences between the outcomes at the end of the period of intervention are as a result of the intervention itself and not of measurement error or the investigator`s mistakes in measuring these outcomes (Schwartz et al., 2004), As the individuals will be assessed twice (after one week and six weeks later) in this thesis, the repeatability between-days has been investigated.

The three-dimensional (3D) gait analysis are reliable and routinely used to measure gait (kinetic and kinematic parameters) to determine any alterations that may take place in the presence of knee OA or other lower limb pathologies (McGinley et al., 2009; Zeni and Higginson, 2009). Previous literature has demonstrated that the repeatability of the gait kinematics and kinetics using a motion analysis system and force platforms in healthy adults was high (Kadaba et al., 1989). They used a Helen Hayes marker set in healthy individuals, sections (3.3.1). In term of one of the primary outcome measures in biomechanically based studies in medial knee OA, the EKAM is the main objective measure. However, to our knowledge, there is only one study that has investigated the consistency of the EKAM to measure the knee load in individuals with medial knee OA (Birmingham et al., 2007). In the current study, we have used a different marker set, the Calibrated Anatomical System Technique (CAST). The main reason behind choosing the CAST marker set compared to Helen Hayes marker set is there could be errors that translate down the limbs in the Helen Hayes marker set such that inaccurate placing of the pelvis markers, could lead to inaccurate foot motion. Secondly, soft tissue artefacts are likely to be greater as markers and wands are placed on the skin (see section 3.4.5.3).

Control of balance during standing (static) and movement (dynamic) is essential and is affected by various components such as physiological changes in the neuromuscular system (muscle weakness),

the aging process, the sensory system, and proprioceptive impairments (Skinner et al., 1984; Doherty et al., 1993; Stevens et al., 2008; Muir et al., 2010). The inability of a body to maintain stable on a supportive base during movement or physical activity is known as a dynamic balance deficit (Gribble et al., 2012) and has been shown to be a risk factor for falls in the elderly (Stalenhoef et al., 2002) and older people with OA (Hoops et al., 2012). The impairments in these components are found in individuals with knee osteoarthritis (OA) causing deficits in balance (Hinman et al., 2002; Lin et al., 2009). Balance is an important attribute in individuals with knee osteoarthritis and a valid and reliable method is needed, which has high confidence and small errors, to allow for use in intervention studies. In medial knee OA studies, the step test has been utilised but in this study, a more dynamic assessment is used called the star excursion balance test (Hinman et al., 2002) and the reliability of this measure has never been assessed in studies with medial knee OA.

3.2. Aims

The aims of this section are to investigate the consistency of the instruments in producing the same results in individuals with medial knee OA at two different points in time separated by at least one week, and to determine the error associated with these measurements so that any difference found between the intervention periods is a true difference.

3.3. Background

3.3.1. Gait analysis

The primary aim of this thesis to investigate the effect of a lateral wedge insole on level of activity, gait kinematics and kinetics, dynamic balance, and ultimately, it is effect on knee pain and function in medial knee OA. One of the primary outcome measures is the EKAM and the factors that affect reproducibility of the external knee adduction moment in gait assessments need to be appreciated.
When assessing gait within the laboratory, there are some external factors that could affect the results such as marker placement, walking speed, or data processing errors (Schwartz et al., 2004). Instability of the markers on bony prominences during the test appeared to be the greatest error in gait analysis (Croce et al., 1997) due to the movement of skin and muscles during gait. One approach that has been suggested to reduce skin movement artefacts is by having markers on rigid clusters (Cappozzo et al., 1996) that are placed on the thigh and shank (Figure 3-1) which have been

demonstrated to show less soft tissue movement than those applied directly to the skin (Angeloni et al., 1992). No previous study has investigated the test-retest repeatability of this marker approach.

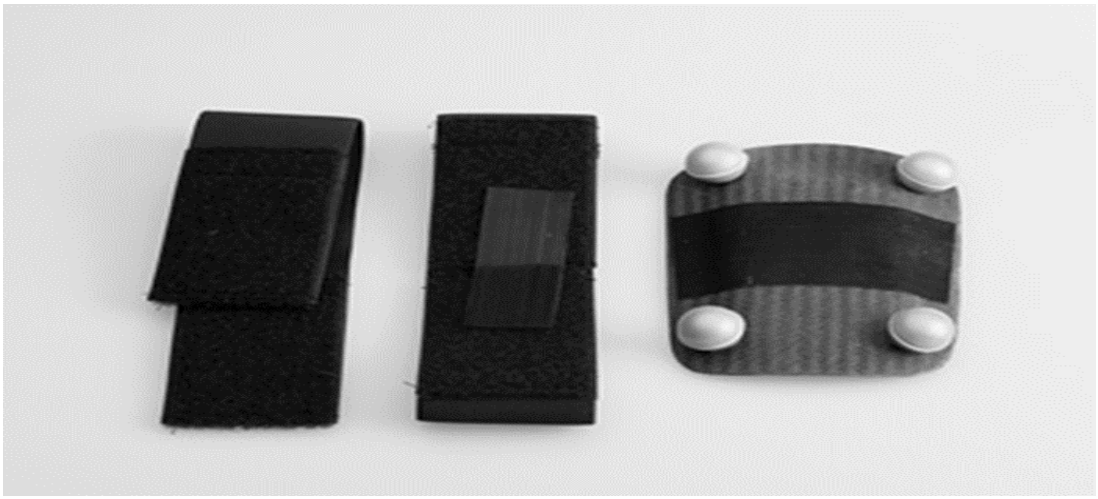


Figure 3-1: Shank cluster with straps for fastening (http://www.qualisys.com)

A previous study by Birmingham et al (2007) investigated the test-retest reliability of the peak knee adduction moment during walking in 31 subjects (21men, 10 women) with medial compartment knee osteoarthritis. They used a modified Helen Hayes marker set which was developed by Kadaba et al (1990) (Figure 3-2). The peak knee adduction was found to be an appropriate outcome for use in studies where interventions aimed to reduce dynamic knee loading on the medial compartment in subjects with medial knee OA (Birmingham et al., 2007).

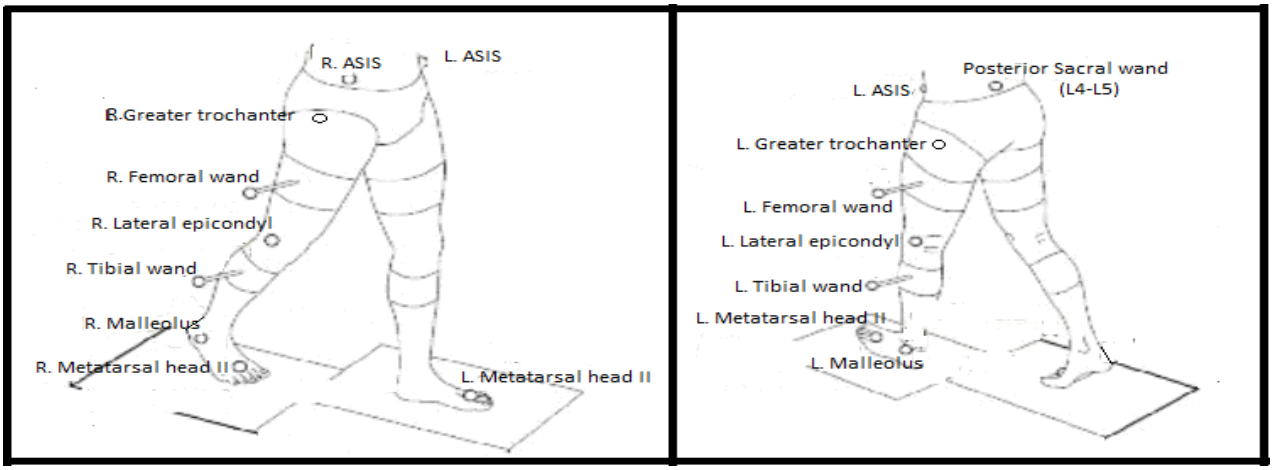


Figure 3-2: Modified Helen Hayes marker set (Kadaba et al., 1990).

They suggested that the intraclass correlation coefficient and the standard error of measurement (SEM) were used to estimate the reliability of the external knee adduction moment. Birmingham and his colleagues (2007) found that ICC of the external knee adduction moment in individuals with medial knee OA during walking was 0.86 and SEM was 0.36 %BW.Ht. In addition, the mean difference in the EKAM between test sessions was 0.1% (Bw×Ht), (two separate test sessions at last 24 hours apart and within 1 week), which indicates an excellent reliability (Birmingham et al., 2007). A similar finding was reported with a previous reliability study that evaluated healthy individuals. Kadaba et al (1989) reported that the EKAM had high reliability when evaluated with 40 healthy individuals on separate days (ICC was 0.9).

3.3.2. Balance

There are several tools that currently exist for measuring balance impairments statically using postural sway test (Hinman et al., 2002) and dynamically using step test (Bennell et al., 2010) or may be by using star excursion balance test in knee osteoarthritis. The postural sway test is commonly used to assess static balance using force platforms (Kollegger etal., 1992), but falls and loss of balance occur during dynamic activities and therefore this is potentially less able to identify individuals at risk of falls due to balance impairments compared to dynamic test (Shumway-Cook et al, 1997 & 2000). In the current literature, the most commonly used test is the step test, whereas the star excursion balance test is another possible method.

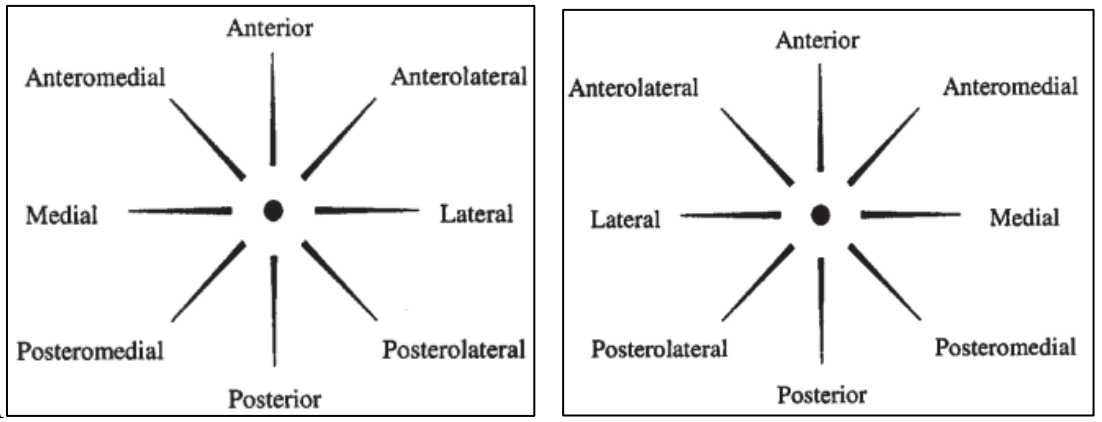
3.3.2.1. Step Test (ST)

The step test (ST) is a common method uses to measure dynamic standing balance in individuals with knee OA (Hinman et al., 2002; Lim et al., 2008, Bennell et al., 2003 & 2010) and developed by Hill (1996). In this test, an individual's ability to place one foot on to a 15cm-high step and then back down on to the ground (double limb support) repeatedly as fast as possible for 15 seconds is assessed. The single leg stance is tested by recording the number of steps taken during this time.

It has been shown that the number of steps significantly decreased ($P< 0.001$) in individuals with knee OA compared to a control group using the ST (Hinman et al., 2002). The ST would only assess dynamic standing balance in one direction (anterior) and neglect the distance between standing base and the 15 cm high step that may play a vital role in body stability during the movement. However, the ST assesses the individuals stepping their foot as fast as they can to evaluate their balance and is a test of endurance rather than functional balance.

3.3.2.2. Star Excursion Balance Test (SEBT)

The Star Excursion Balance Test (SEBT) is a simple, inexpensive test, used to measure dynamic balance (Gribble et al., 2012) that incorporate a single-leg stance with maximum reach of the other leg (Olmsted et al., 2002). It is performed by measuring the maximal distance that will be reached by one leg in different directions, and then returning slowly to the starting position (double support) while keeping balance throughout the test (Olmsted et al., 2002; Gribble et al., 2007). The directions relative to the supporting leg on the platform are; anterior (A), anterolateral (AL), anteromedial (AM), posterior (P), posterolateral (PL), posteromedial (PM), medial (M), and lateral (L), and the difference between them equals 45˚(Olmsted et al., 2002) (Figure 3-3).



A B

Figure 3-3: Eight reaching directions (A) Right leg stance (B) Left- leg stance (Gribble & Hertel, 2003).

Evidence has recommended doing four practice trials followed by three test trials in each of the eight directions because the learning effect was found in the first four trials (Robinson and Gribble, 2008a; Munro and Herrington, 2010). However, focusing the assessment to specific directions that are performed by certain muscles is a potential method to save time (Olmsted et al., 2002; Herrington et al., 2009). The anterior and medial directions will be proposed for testing with knee OA patients because the quadriceps muscle and gluteus medius muscle are the most affected in knee OA and become weak (Slemenda et al., 1997; Chang et al., 2005).

3.4. Method

3.4.1. Sample size

The sessions were all completed at the University of Salford Gait Laboratory which has a strong record in musculoskeletal research and clinical gait analysis. The Research Ethics Panel (REP) of the Academic Audit and Governance Committee at the University of Salford approved the study (HSCR14/07). Ten subjects who have been diagnosed with medial tibiofemoral OA were recruited in this study. The participants were postgraduate students, staff at University of Salford, and volunteers who live in Manchester and accepted our invitation.

The participants were recruited through; an invitation letter that was sent directly to the participants have who have knee OA and posters that were attached to notice boards in most university buildings. The subjects who met the following inclusion and exclusion criteria were asked to consider taking part and signed the informed consent forms.

3.4.2. Inclusion criteria:

To define medial knee OA, a participant must have met all of the following; their ages between 40-85 years where upper age limit due to the amount of walking involved in the study. If they complain of Pain with walking (using KOOS question), they need to have at least mild pain walking on a flat surface - clinical diagnosis by qualified clinician. If the participants were diagnosed with mild-moderate medial knee OA by GP based on the clinical and radiographic criteria, using Kellgren and Lawrence scale (K/L) (Kellgren and Lawrance, 1975), and according to the criteria of the American College of Rheumatology (ACR) (Altman et al., 1986). (KL grade 2 or 3 in the tibiofemoral joint (TFJ) knee OA is usually classified (Felson et al., 1997). If they complain of medial tenderness either by their own indication that this is where they have pain or by examination showing tenderness at the medial TF joint line – Clinical diagnosis by qualified clinician. Absence of PF tenderness on examination. They are able to walk for 100 meters non-stop - participant response, speak and understand English to read the information sheet and sign consent form and they can walk without any walk assistive.

3.4.3. Exclusion criteria:

Participants were be excluded if the pain is more localized to the patellofemoral joint on examination than medial joint line, have tricompartmental knee osteoarthritis or have grade 4 medial tibiofemoral osteoarthritis on the Kellgren Lawrence scale. Other exclusions include a history of high tibial

osteotomy or other realignment surgery or total knee replacement on the affected side. In addition, a history of Knee Arthroscopy with the last 6 months, Intra-articular injection into the treatment knee in the last 3 months, any foot and ankle problems that will contraindicate the use of the footwear load modifying interventions, or inflammatory arthritis including Rheumatoid Arthritis. If the participants complain of complex pain conditions such as Diabetic Neuropathic pain, fibromyalgia. The participants were excluded if they have severe coexisting medical morbidities, or currently use, or have used, orthoses of any description prescribed by a Podiatrist or Orthotist within the last 2 months. If the participants cannot understand procedures, unable to walk unaided and have to rely on a stick, crutch or frame, or cannot walk for 100 meters without stopping they were also be excluded, as they may be unable to complete the full testing protocol.

3.4.4. Balance assessment procedure

Each participant was instructed to change into a T-shirt and shorts to perform the tests freely and without any restriction due to their clothes. Participants were not permitted to wear any shoes to remove any factors that could impact on their balance and could not use hand support during the test. After taking the demographic details, the participants were asked to undertake the following tests randomly with one-hour gap between them to minimize any fatigue.

3.4.4.1 Star Excursion Balance Test (SEBT) procedure

A modified SEBT device was used to assess dynamic balance in individuals with medial knee OA. This device uses the same principle as the original SEBT that was described by the previous studies (Kinzey and Armstrong, 1998; Robinson and Gribble, 2008; Munro and Herrington, 2010). Instead of taping lines on the ground as in the original version (Figure 3-4a), a movable platform with a long bar and a small block on the bar is used to determine the reach distance that gain by the participants (Figure 3.4b). Evidence has recommended performing four practice trials followed by three test trials in the eight directions to remove the learning effect (Robinson and Gribble, 2008; Munro and Herrington, 2010).

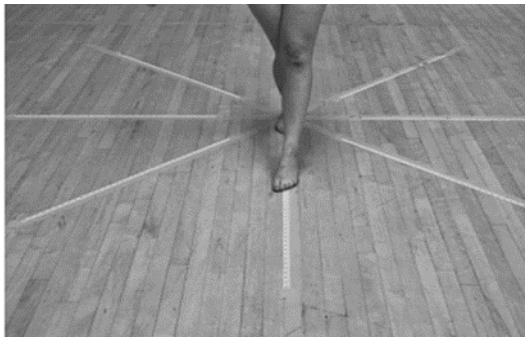
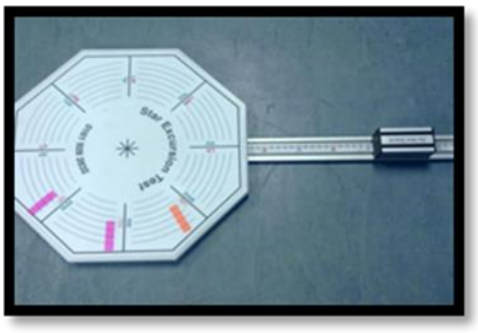
a   b

Figure 3-4: (a) Original SEBT (b) Modified SEBT (Munro and Herrington, 2010).

Participants stood barefoot on the middle of the platform and were asked to slide the indicator (block) on the bar as far as possible using the distal part of their other foot. Participants stood facing the bar for the anterior direction and stood with their side to the bar for the medial direction. Then, participants performed this test 7 times (4 times practice and 3 times as a test) for each direction (anterior and medial) (Figure 3-5). The reach distance was recorded in centimeters and then participants returned their foot to the platform (double stance) without losing their balance. The trials were considered successful if the participants pushed the block and did not stop on it, did not push the block suddenly and/or quickly, and did not touch the bar or floor while returning to the platform. If they did any of these, the test had to be repeated. The tested leg was chosen randomly and each leg was tested in different directions before switch to other leg to minimise fatigue. The foot position was identified accurately on the platform and recorded to help determine the correct position (same position) for the other leg and for the second session with aligning the heel with the centre of the grid and great toe with the anteriorly projected line. The participants were instructed to keep the heel of the stance foot on the platform with hands free. The same procedure and order was followed in the second session.

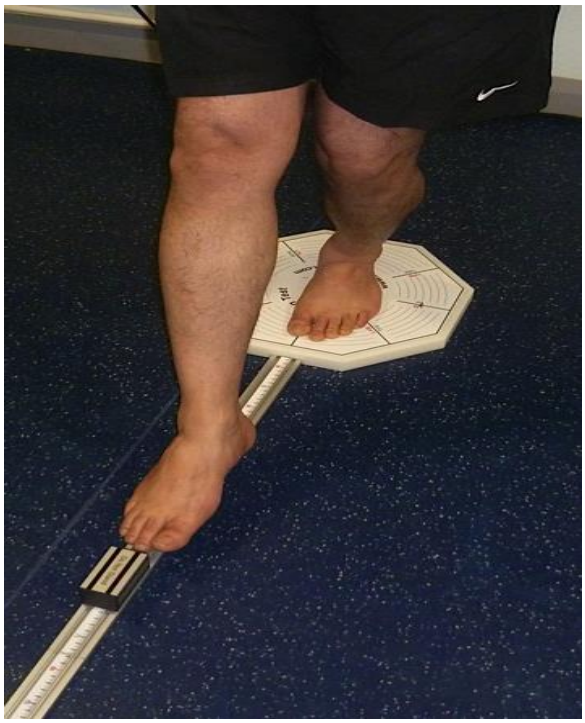
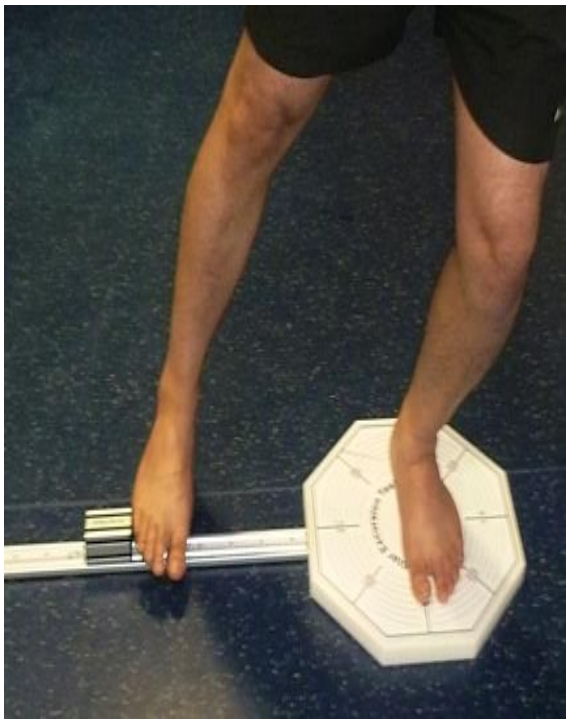
a   b

Figure 3-5: Star excursion balance test for left limb (a) anterior direction, (b) medial direction.

Limb length has been found to be correlated significantly with reach distance, therefore normalized excursion distance was used (Gribble and Hertel, 2003). The normalized balance distance was calculated by dividing the distance reached by the individual's limb length (distance between anterior superior iliac supine and medial malleolus) and multiplying by 100 (Gribble and Hertel, 2003).

3.4.4.2. Step Test (ST) procedure

The supporting limb was chosen randomly and the test was performed once only with one practice trial before the test to avoid any potential muscle fatigue. Two sides were tested with one-minute rest between them. To perform the ST, the participants stood on one leg while stepping the contralateral foot onto a 15 cm step up and then back down to the floor repeatedly as fast as possible for 15 seconds (Hill, 1996) (Figure 3-6). The investigator stood beside the participants to hold them if they lose their balance during the test and zero was recorded if this occurred. The number of times the participants stepped their foot up and down was recorded.

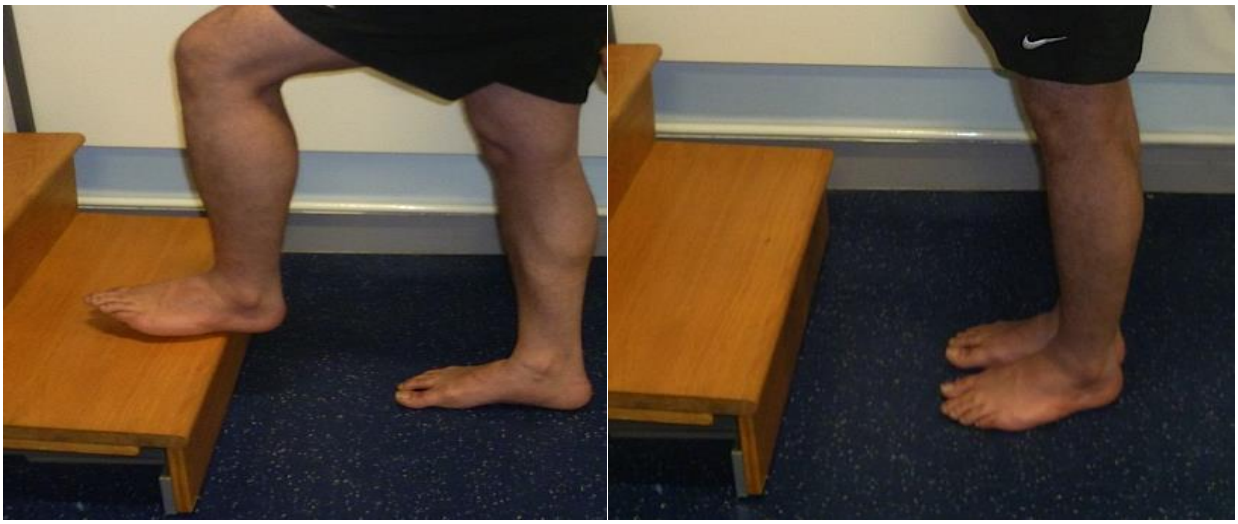


Figure 3-6: Step test, participant stood on the affected leg (Right).

3.4.5. Gait analysis procedure

3.4.5.1. Equipment

Gait assessment and testing was conducted at the podiatry laboratory at the University of Salford. For kinematic data collection, a 16 Oqus 300 infra-red cameras (Qualisys AB, Gothenburg, Sweden) sampling at 100Hz were used to capture the location of the reflective markers which were placed on the participant`s limbs during the test stages. Kinetic data were collected using four force platforms (BPA400600, AMTI: Advanced Mechanical Technology Incorporation, Watertown, USA) sampling at 1000 Hz. These force platforms lie within the walkway (10 metres long, 2 metre wide). (Figure 3-7).

Figure 3-7: The gait laboratory with 16 infra-red cameras (Qualisys Oqus motion analysis system) and four force platforms.

The 16 infrared cameras had to be positioned and adjusted in proper position around the walkway in podiatry gait laboratory to give the best possible view of the markers during trials to achieve complete data collection. All 16 cameras were then checked to ensure that all markers are detectable in the camera`s field.

3.4.5.2. System calibration

System calibration was performed in two steps. A static calibration was performed to determine the position and orientation of the 16 cameras in relation to the global co-ordinates system of the laboratory using L-Frame with four reflective markers which were placed onto the corner of the force plate, with the arms parallel to the edges of the plate (Figure 3-8).

Figure 3-8: L-shaped metal frame with four markers.

Secondly, a dynamic calibration was performed to calibrate the walkway volume, so any motion in the measurement volume would be recorded, by waving the T-shaped wand which has two reflective markers (Figure 3-9), throughout the walkway for 60 seconds. The distance between the markers is 750.43mm.

Figure 3.9: T-shaped wand with two markers.

The laboratory co-ordinate system is represented by the L-Frame, which consisted of the following axes; X is the anterior/posterior axis, Y is the medial/lateral, and Z is the vertical axis. In this study, the positive X-axis points anteriorly (forward), the positive Y-axis points medially (to the left), and the positive Z-axis points upward. Once the calibration procedures had been completed, the calibration residual results showed whether the calibration has been successful or not. Therefore, the results for each camera must be below 1mm, and the standard deviation of the wand length must be below 1mm to be acceptable and the calibration to be considered successful.

3.4.5.3. Location of reflective markers

To calculate the kinematics, the position and orientation of the body segments (POSE) are identified using retro-reflective markers. Cappozzo et al., (1996) found that the skin movement artefacts (movement between markers and underlying bone) were a major error during the walking trial. Therefore, the Calibrated Anatomical System Technique (CAST) method was used in the current study to minimise skin movement artefacts by using rigid cluster plates (Cappozzo et al., 1995 & 1996). This technique relies on determining the POSE using anatomical markers (the individual markers positioned over bony prominences) and technical markers (the cluster markers positioned over fleshy areas). The anatomical markers are only essential during the static trial to determine the positions and axes of the joints while the technical markers are fixed over fleshy areas to track the motion of bones during the dynamic trial. Therefore, this technique decreases the skin movement artefacts as the displacement error of the markers is greater over bony prominence than over fleshy areas (Cappozzo et al., 1996).

3.4.5.4. Biomechanical model

As previously mentioned, a different markers set has been used in this study when compared to a previous gait study which was performed by Birmingham et al (2007). They used the conventional gait model (modified Helen Hayes marker set) which uses 15 markers to define body segments (Davis et al, 1991b, Kadaba et al, 1990). In the conventional gait model markers set, a minimal number of markers have been used with a large distance between them, only three rotational degrees of freedom for the hip and knee and two degrees of freedom for the ankle are used, and the anatomical markers are used to track the segments in this method (Cappozzo et al., 2005). Therefore, this method is potentially more affected by skin movement artefacts and is very sensitive to any noise in the data (Cereatti et al., 2007). In addition, only two tracking markers are used in the conventional gait model to provide each segment, which means that the movement of the distal segment depends on the proximal segments (Kadaba et al, 1990). This means that identifying the position and orientation of a segment independently of other segments is impossible. So, in the Helen Hayes model, any error is transferred from a segment to the other and introduces increased measurement error (Schwartz et al., 2004).

Therefore, considering the previous reasons, a six degrees of freedom (6DOF) marker set model was applied in this study whereby four retro-reflective markers are attached to a rigid segment are used to track the segment (movement of the segment) and each frame of data specifies the position and orientation of the segment. Each joint (or each segment) is determined independently using 6DOF, meaning it has three translational (vertical, anterior/posterior, medial/lateral), and three rotational (transverse, sagittal, frontal) motions. The motion of rigid segments can be fully described by measuring three independent translational DOF (position) and three independent rotational DOF (orientation). Therefore, each segment is calculated independently and thereby some of the errors which were introduced by the previous model have been decreased by using 6DOF and clusters (Cappozzo et al, 1996; Cereatti et al., 2007).

3.4.5.5. Collection of kinematics and kinetics data

Infra-red is released from light emitting diodes (LEDs) by the 16 Oqus cameras. Infra-red is then reflected from the markers back to the camera thus giving the two dimensional point of each marker. Then, the composed two-dimensional co-ordinates and the relative position of the cameras to the laboratory co-ordinate system calculate the three-dimensional co-ordinate. For the three-dimensional position, each marker must be identified by at least two cameras during the trial

(Cappozzo et al., 2005). At least, three retro-reflective markers on each cluster must be detected clearly by the cameras to determine the position and orientation of the body segment. The nearby body segment is determined by the same way and the angle between them is calculated, for example; range of motion (Kaufman and Sutherland, 2006).

3.4.5.6. Gait data collection procedure

The gait laboratory and equipment at the University of Salford were prepared, checked, and calibrated (see section 3.4.4.2.) before each session to ensure they worked appropriately to collect the data.

3.4.5.6.1. Participants preparation

Once the participant arrived at the gait laboratory, the whole study and the procedure were explained in full and once the participant was familiarised with the testing procedures and happy, the consent form was been completed and signed after answering any questions the participants still had. Each participant was then asked to wear shorts and a comfortable T-shirt. Height and mass were measured and recorded and then given standard shoes (Ecco Zen, Figure 3-10) to wear.

Figure 3-10: Standard insole (Ecco Zen).

Following this, Forty-four anatomical and technical (tracker) retro-reflective markers (14 mm diameter) were placed on the skin of the lower limbs using hypoallergenic double sided adhesive tape (Figure 3-11).

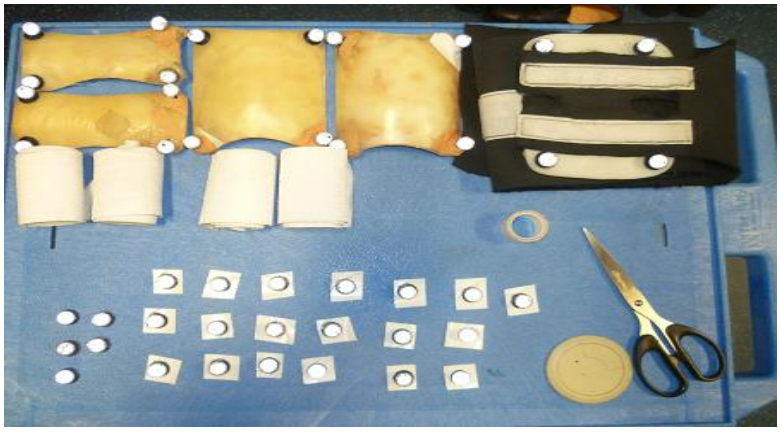


Figure 3-11: Retro-reflective markers, cluster pads, bandages, and hypoallergenic double sided adhesive tape.

In standing, anatomical markers and technical markers were attached bilaterally to the lower limbs of the participant using hypo-allergenic adhesive tape and Fabiofoam SuperWrap bandages. Anatomical markers were fixed at anterior superior iliac spines (ASISs), posterior superior iliac spines (PSISs), iliac crests, right and left greater trochanters, lateral and medial femoral epicondyles, and lateral and medial malleoli. For technical markers, four rigid plastic clusters with four markers on each (orientation and distance between markers are fixed) were attached to the pelvis, thigh, shank using Fabiofoam SuperWrap bandages to ensure that migration of these pads down the limbs is avoided. Four retro-reflective markers (on 1st, 2nd, 5th metatarsal, and calcaneus) were glued onto shoes, which is assumed to act as a rigid body, and will reduce markers displacement during the trial. In total, 44 retro-reflective markers were placed on the participants (16 anatomical markers and 28 technical markers) (Figure 3-12).

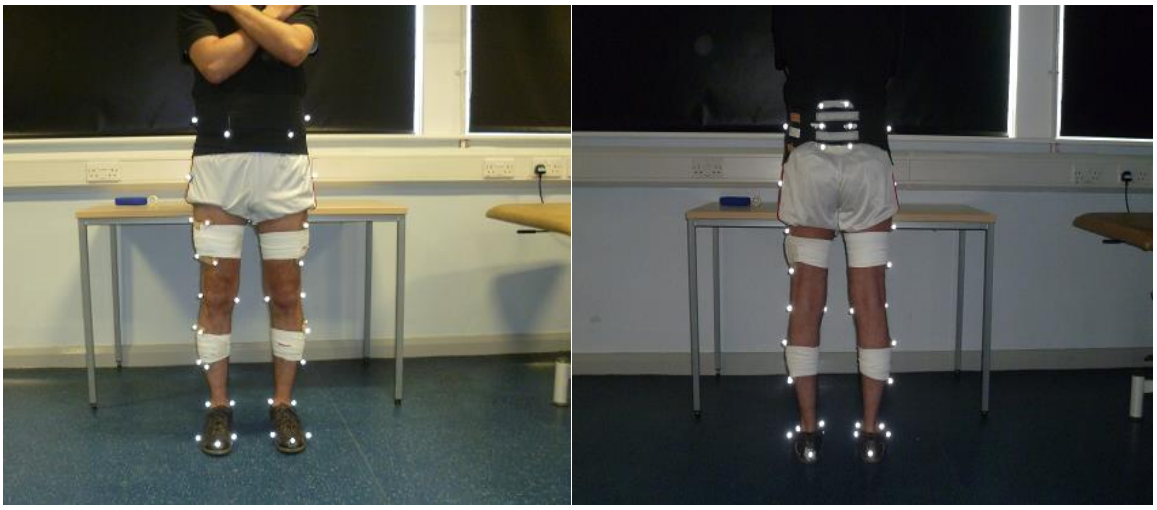


Figure 3-12: Anatomical and technical markers (anterior and posterior views).

These markers were placed on the participant through palpation by the physiotherapist (main investigator) following measurement of the distance between each marker to identify the exact location of the markers and to improve the accuracy of their position between two sessions (Figure 3-13), this method is a similar version to what was used by Jones (2010).

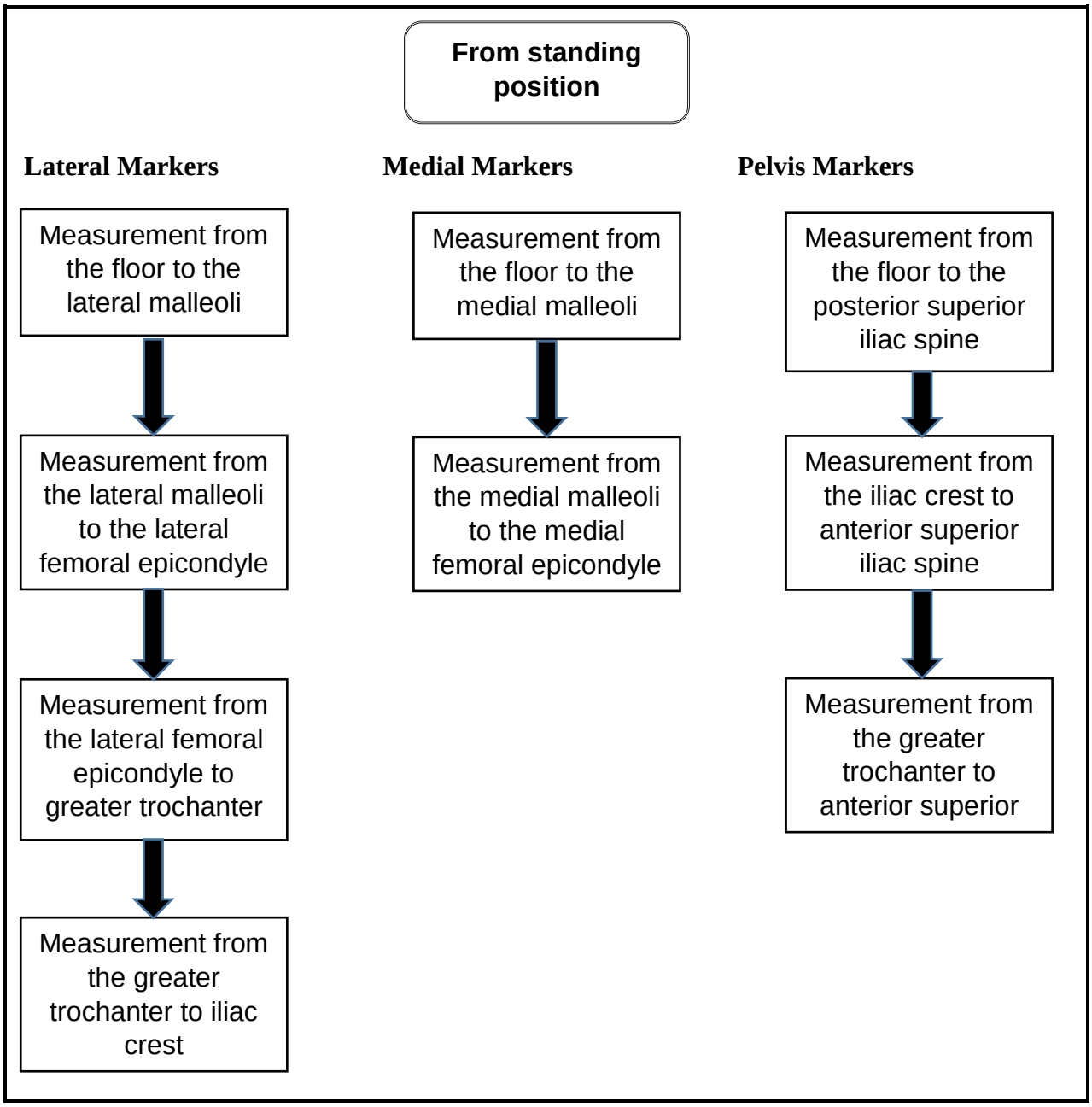


Figure 3-13: Anatomical markers location measurement for between-day test.

3.4.5.6.2. Test procedure

Prior to data collection, height and mass were measured and the standard shoes (ECCO Zen) (without insoles) were worn by the participant. Then, for static trial, the participant was asked to stand on a force platform for 10 seconds and static images (three-dimensional) were obtained from the sixteen infra-red cameras. All markers must be identified by the cameras and anatomical reflective markers were removed leaving only the cluster plates on the shank, thigh and pelvis (technical markers) to decrease skin movement artefacts (Cappozzo et al., 1996). The participant was then asked to walk 10 times at a self-selected walking speed through walk-way. Five successful trials (participant`s foot must strike the force platform, complete stance by one foot within one force

platform) were analysed. The trial was considered successful if the participants touch each force platform with one foot and the whole foot must strike the force platform in the middle. However, if the two feet touch the same platform or the edge of the force platform, this would result in a measurement error of the ground reaction force, so the trial was repeated. The participants were not informed about the force plates to prevent altering their gait pattern. This test procedure was repeated after a week with the same procedure (between-days).

3.4.5.7. Data processing

The collected data were processed using Qualisys Track Manager (QTM) software (Version 2.9), and Visual3D (V3D) software (Version 5.01.23, C-Motion Inc, Rockville, MD, USA), Microsoft Excel 2010 (Microsoft, Washington, USA), and SPSS (Version 20, IBM Corporation) respectively. Firstly, each marker was labelled for each walking trial (successful five trials) for each participant using QTM (figure 3-14a). These walking trials (c3d) were exported to V3D to create biomechanical model and report (figure 3-14b).

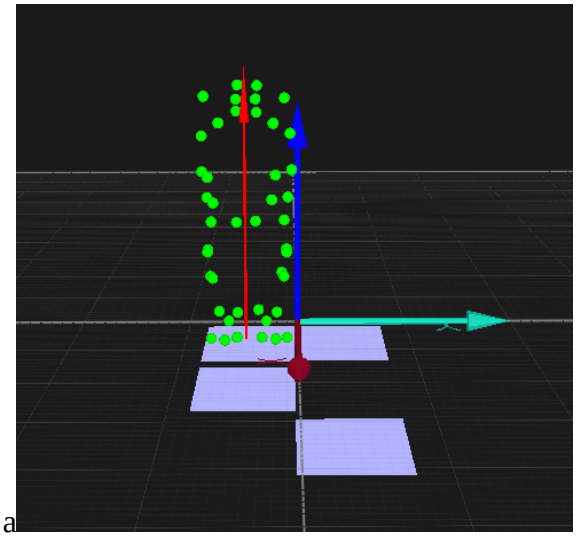
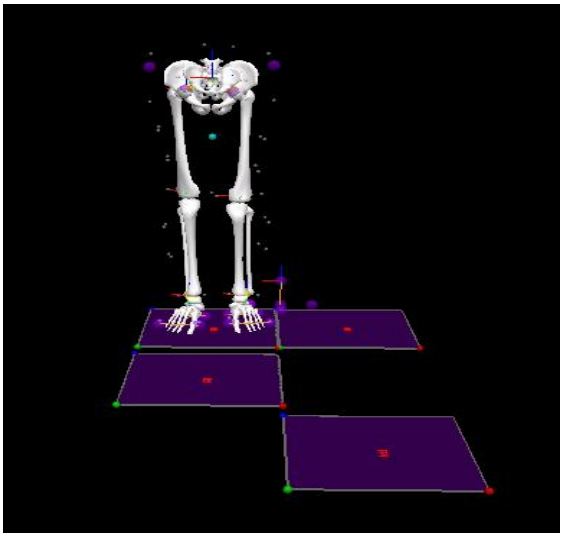
a   b

Figure 3-14: (a) Qualysis Track Manager, (b) Visual 3D Model.

The model is referred to as a six degree of freedom (6DOF) model due to having six variables; three variables describe segment translation in three orthogonal axes (vertical, anterior/posterior, medial/lateral) and three variables describe the rotation about each axis (transverse, sagittal, frontal) to describe the POSE in 3D space. The 6DOF biomechanical model was built where the participants' height (m) and body mass (kg) were entered. The biomechanical model was defined (Table 3-1) to determine the proximal and distal joints and tracking markers. The hip joint centre was calculated based on the anterior and posterior superior iliac spine markers whilst knee and ankle joint centres were calculated as midpoints between the malleoli and femoral epicondyles, respectively.

Table 3-1: Segments, proximal & distal joint and tracking markers

segment	Proximal joint	Distal joint	Tracking markers
Pelvis	• Right anterior superior iliac spine • Left anterior superior iliac spine	• Right posterior superior iliac spine • Left posterior superior iliac spine	Pelvis cluster belt (4 markers)
Thigh	• Hip joint centre	• Medial femoral condyle • Lateral femoral condyle	Thigh cluster (two clusters; 4 markers for each)
Shank	• Medial femoral condyle • Lateral femoral condyle	• Medial malleolus • Lateral malleolus	Shank cluster (two clusters; 4 markers for each)
Foot	• Medial malleolus • Lateral malleolus	• 1st metatarsal head • 5th metatarsal head	

Following the creation of the biomechanical model, the raw kinematic data was interpolated with a maximum gap fill of ten frames. The data were then low-pass filtered to minimise the noise, remove the high frequency component, and retain the movement signal because the movement signal is limited to a band of low frequencies. Cut-off points of 6Hz for kinematics (Winter, 2009) and 25Hz for kinetics (Schneider and Chao, 1983) were used to filter the data using Butterworth fourth order method (Schneider and Chao, 1983; Winter, 2009). Normalised stance phase was applied for the kinetic data whereas normalised gait cycle was used for kinematic data. Each gait variable of interest was exported from V3D to Microsoft Excel 2010. Discrete values such as the maxima and minima of the kinematic and kinetic data were also extracted.

3.4.6. Statistical analysis

As the planned study will investigate the effect of lateral wedged insoles on several outcomes in individuals with medial knee OA, this study has been undertaken to ensure that the differences between outcomes at the end of the intervention are a result of the intervention itself and not of measurement errors or investigator's mistakes in measuring the outcomes. Therefore, an analysis was performed to determine the consistency of kinematic and kinetic parameters during walking in individuals with medial knee OA in between two different sessions (between-day).

Mean, Standard Deviation (SD), Standard Error of Measurement (SEM), and Intra-class Correlation Coefficients (ICC) were used to assess the test-retest reliability, which is the consistency of the results. The mean is the average of data whereas the SD is a measure of data variability around the mean. SEM is used to determine absolute reliability and was calculated by using the following formula: SEM = SD*√ (1-ICC) (Harvill, 1991; Thomas et al., 2005). A lower SEM demonstrates better reliability (Baumgartner, 1989), and therefore the researcher can estimate the range of true improvement by eliminating the percentage error. The ICC (3k), two-way mixed model to measure the average of reliability, is a measure of consistency of measurements, and it is classified to describe the range of ICC values as following criteria; more than 0.75 is excellent, from 0.4 to 0.75 is fair to good, and less than 0.4 is poor reliability (Fleiss, 2011). The Minimal Detectable Difference (MDD) uses to define that amount of change in a variable that must be achieved to reflect a true difference and it was calculated using the formula; 1.96 * SEM * 1.4142 (Kean et al., 2010). This value is required to detect the minimal change which will be considered clinically significant and the greater the reliability of the measurement, the smaller the MDD (Kropmans et al., 1999). In addition, for gait data, Coefficients of Multiple Correlation (CMC), the shapes of the waveforms, were used to measure the strength of similarities of each variable and compare each joint angle and moment waveform (Kadaba et al, 1989). CMC can be any value from zero (0) to positive one (+1). The closer the result is to one, the higher the reliability. According to Growney et al., (1997), similar waveforms with values more than 0.8 demonstrate high test-retest reliability. The CMC was used by Kadaba et al., (1989). All statistics were performed using The Statistical Package for the Social Sciences (SPSS 20, IBM, New York, USA). However, SEBT and ST are two different instruments measuring dynamic balance, therefore the Bland and Altman Plots test and Kappa test were not calculated. The reason those tests are not applicable is that they measure dynamic balance in different unites. The SEBT measures the reached distance by centimetre and the ST measures the absolute number of steps up and down.

3.5. Results

The current study investigated the repeatability of gait kinematic and kinetic data, step test, and star excursion balance test in individuals with medial knee OA. The participants performed the tests at two sessions with one week apart.

3.5.1. Participants

Ten participants with confirmed medial knee OA were recruited in this study (9 males, 1 female) completed the study with the mean and standard deviation (SD) shown in Table 3-2.

Table 3-2: Demographics of the participants

Subjects	**Gender**	**Age** (years **)**	**Affected Knee**	**Height** (cm)	**Mass** (kg)	**Body Mass Index** (kg/m²)
1	M	42	L	167.5	87	31.01
2	M	43	R	168	82	29.05
3	M	44	L	164	70	26.03
4	F	40	R	168	67	23.74
5	M	42	L	173	88	29.40
6	M	43	L	177	92	29.40
7	M	44	R	184	99	29.24
8	M	53	L	179	85	26.53
9	M	51	L	181	93	28.39
10	M	53	R	171	80	27.36
Mean (±SD)	9 M, 1F	46 (±4.88)	6 L, 4 R	173 (±6.68)	84.3 (±10)	28 (±2.12)

3.5.2. Test-retest reliability of gait kinematic and kinetics

Walking speed did not differ significantly between sessions (p=0.37). The mean and SD of CMC of joint range of motions (ROM), moments and ground reaction forces (GRF) are presented in Table 3-3 and Table 3-4. The results demonstrated excellent reliability in the majority of the gait kinematic and kinetic data in individuals with medial knee OA with CMC >0.91, whereas the lowest CMC was for foot progression with 0.68.

Table 3-3: Mean, SD of the coefficient of multiple correlation (CMC) of joint range of motion (ROM) for all participants in shod condition.

	Mean	SD*
Hip angle –y	0.97	0.04
Hip angle –z	0.91	0.06
Knee angle –y	0.97	0.03
Knee angle –z	0.94	0.08
Ankle angle –y	0.94	0.05
Ankle angle –z	0.82	0.08
Hip angle –x	0.99	0.01
Knee angle –x	0.99	0.01
Ankle angle –x	0.98	0.01
Foot progression –z	0.68	0.13

*SD= Standard Deviation
X (sagittal) =Flexion/ Extension, Y (frontal) = Abduction/Adduction, Z (transverse) = Internal/ External Rotation

Table 3-4: Mean, SD of the coefficient of multiple correlation (CMC) of moments and ground reaction force for all participants in shod condition.

	Mean	SD*
Hip Moment –x	0.97	0.01
Hip Moment –y	0.98	0.01
Knee Moment –x	0.93	0.04
Knee Moment –y	0.98	0.01
Ankle Moment –x	0.99	0.01
Ankle Moment –y	0.81	0.11
GRF- z	0.99	0.01
GRF –y	0.99	0.01

*SD= Standard Deviation
X (sagittal) =Flexion/ Extension Y (frontal) = Abduction/Adduction Z (transverse) = Internal/ External Rotation

The mean, SD, SEM, MDD and ICC of kinetic and kinematic parameters for hip, knee, and ankle in individuals with medial knee OA are shown in Table 3-5, Table 3-6. The results for hip moments and angles demonstrated high between-day reliability with the ICC ranging from 0.699-0.988, the SEM ranging from 0.01- 0.10 Nm/kg and 0.10˚-0.46˚ with MDD 0.02-0.28 Nm/kg and 0.29˚-1.26˚ for hip moments and angles, respectively. Kinetic and kinematic parameters for knee joint including KAAI showed excellent test-retest reliability with the ICC ranged from 0.89-0.99 and the SEM ranging from 0.01- 0.03 Nm/kg and 0.11˚-1.14˚ with MDD 0.02-0.07 Nm/kg and 0.29˚-3.15˚ for knee moments and angles, respectively. The results for ankle moments and angles demonstrated high between-day reliability with the ICC ranging from 0.922-0.99 the SEM ranging from 0.01- 0.05 Nm/kg and 0.10˚-0.46˚ with MDD 0.02-0.13 Nm/kg and 0.42˚-2.74˚ for ankle moments and angles, respectively. The foot progression demonstrated excellent reliability (ICC > 0.988), the SEM ranging from 0.15˚-0.23˚ with MDD ranging from 0.42˚ and 0.63˚. The reliability of the ground reaction forces was excellent with ICC >0.91, SEM<0.01. Bw and MDD<0.02 .Bw. The between-day reliability of the EKAM, which used in the main study as a primary outcome, is excellent where the ICC was 0.99 with small SEM and MDD, 0.002 Nm/kg and 0.01 Nm/kg, respectively, in individuals with medial knee OA.

Table 3-5: Mean, standard deviation (SD), Standard error of measurement (SEM), Minimal detectable difference (MDD), and Intraclass correlation coefficient (ICC) of kinetic parameters for hip, knee, and ankle in all individuals.

		Mean (±SD)	SEM	MDD	ICC*
Hip Moment –x (Nm/kg)	max	1.00 (±0.15)	0.03	0.08	0.954
	Min	-0.71 (±0.07)	0.02	0.04	0.946
Hip Moment –y (Nm/kg)	peak1	0.77 (±0.05)	0.01	0.02	0.988
	trough	0.59 (±0.43)	0.06	0.16	0.98
	peak2	0.69 (±0.45)	0.10	0.28	0.949
Knee Moment –x (Nm/kg)	max	0.52 (±0.08)	0.02	0.04	0.957
	min	-0.56 (±0.08)	0.03	0.07	0.89
Knee Moment –y (Nm/kg)	peak1	0.52 (±0.03)	0.002	0.01	0.994
	trough	0.31 (±0.03)	0.01	0.02	0.968
	peak2	0.44 (±0.03)	0.01	0.02	0.98
Ankle Moment –x (Nm/kg)	max	1.51 (±0.04)	0.05	0.13	0.989
	min	-0.19 (±0.03)	0.01	0.02	0.942
Ankle Moment –y (Nm/kg)	max	0.14 (±0.03)	0.05	0.13	0.971
	min	-0.13 (±0.04)	0.01	0.03	0.946
GRF- z (*BW)	Max Fz1	1.09 (±0.03)	0.01	0.02	0.958
	Min Fz2	0.79 (±0.02)	0.004	0.01	0.966
	Max Fz3	1.07 (±0.02)	0.01	0.02	0.914
GRF –y (*BW)	Min	-0.13 (±0.01)	0.01	0.02	0.995
	Max	0.16 (±0.01)	0.01	0.02	0.997
KAAI (Nm/kg)*s		0.24 (±0.06)	0.01	0.03	0.979

X (sagittal) =Flexion/ Extension Y (frontal) = Abduction/Adduction Z (transverse) = Internal/ External Rotation
*Significant value $P<0.05$

Table 3-6: Mean, standard deviation (SD), Standard error of measurement (SEM), Minimal detectable difference (MDD), and Intraclass correlation coefficient (ICC) of kinematic parameters for hip, knee, and ankle in all individuals.

		Mean (±SD)	SEM	MDD	ICC*
Hip angle –y (degree)	max	4.42 (±0.56)	0.12	0.32	0.956
	min	-10.22 (±0.59)	0.13	0.36	0.952
	ROM	14.62 (±0.83)	0.46	1.26	0.699
Hip angle –z (degree)	max	-2.99 (±1.02)	0.29	0.72	0.936
	min	-19.12 (±0.72)	0.14	0.40	0.96
	ROM	16.13 (±1.21)	0.25	0.70	0.957
Knee angle –y (degree)	max	6.05 (±0.47)	0.17	0.46	0.879
	min	-11.30 (±0.86)	0.22	0.60	0.937
	ROM	17.35 (±1.03)	0.28	0.78	0.925
Knee angle –z (degree)	max	9.36 (±1.07)	0.26	0.72	0.941
	min	-12.52 (±1.27)	0.29	0.80	0.948
	ROM	21.88 (±1.64)	0.24	0.67	0.978
Ankle angle –y (degree)	max	5.87 (±1.03)	0.15	0.42	0.978
	min	-8.19 (±0.97)	0.29	0.58	0.954
	ROM	14.06 (±1.62)	0.26	0.73	0.974
Ankle angle –z (degree)	max	8.25 (±1.47)	0.28	0.78	0.963
	min	-4.45 (±1.40)	0.29	0.58	0.978
	ROM	12.70 (±1.75)	0.44	1.23	0.936
Hip angle –x (degree)	Max Flexion1	33.11 (±1.12)	0.19	0.54	0.97
	Min Flexion	-2.73 (±0.75)	0.10	0.29	0.981
	Max Flexionx2	38.85 (±1.07)	0.24	0.65	0.951
	ROM	41.58 (±1.34)	0.16	0.44	0.986
Knee angle –x (degree)	IC	2.65 (±1.56)	0.42	1.17	0.927
	Loading Respond	15.98 (±1.56)	0.32	0.90	0.957
	Mid-stance	6.94 (±0.95)	0.39	1.07	0.834
	Term. Stance	43.67 (±3.26)	1.14	3.15	0.878
	Mid-swing	71.53 (±1.22)	0.18	0.50	0.978
	ROM	64.59 (±0.81)	0.11	0.29	0.983
Ankle angle –x (degree)	IC	3.57 (±1.04)	0.99	2.74	0.991
	Loading Respond	-4.72 (±0.88)	0.21	0.57	0.945
	Max Dorsiflexion	20.34 (±0.86)	0.24	0.67	0.922
	Min Dorsiflexion	-11.49 (±1.67)	0.25	0.69	0.978
	ROM	31.83 (±1.64)	0.27	0.75	0.973
Foot Progression-z (degree)	max	13.57 (±1.71)	0.15	0.42	0.992
	min	2.64 (±2.07)	0.23	0.63	0.988

X (sagittal) =Flexion/ Extension Y (frontal) = Abduction/Adduction Z (transverse) = Internal/ External Rotation.
*Significant value P<0.05

3.5.3. Test-retest reliability of dynamic balance test

The mean, SD, SEM, 95%CI, MDD, and ICC of the SEBT and ST for the affected and contralateral sides are presented in Table 3-7, 3-8, and 3-9.

3.5.3.1. Star excursion balance test

The results show that the raw excursion distance demonstrated excellent test-retest reliability (Table 3-7). The ICCs were 0.927 and 0.966, the SEMs were 1.25 cm and 1.17 cm, and the MDDs were 3.47 cm and 3.24 cm for the anterior and medial direction, respectively, in the affected side. Moreover, ICCs were 0.931 and 0.929, SEMs were 1.06 cm and 1.39 cm, and the MDDs were 2.93 cm and 3.85 cm for the anterior and medial direction, respectively, for contralateral side which indicated excellent reliability.

Table 3-7: Raw balance excursion of SEBT

Side	Direction	Mean		SD	95% CI	SEM (cm)	MDD (cm)	ICC
		Session 1	Session 2					
Affected (cm)	Anterior	71.42	70.40	4.64	68.04-73.78	1.25	3.47	0.927*
	Medial	70.96	70.43	6.34	66.77-74.62	1.17	3.24	0.966*
Contralateral (cm)	Anterior	75.16	75.33	4.02	72.75-77.74	1.06	2.93	0.931*
	Medial	73.93	74.16	5.21	70.82-77.28	1.39	3.85	0.929*

*Significant value P<0.05

In the normalised excursion distance (Table 3-8), ICCs were 0.962 and 0.981, SEMs were 1.73% and 1.53%, and the MDDs were 4.80 % and 4.24 % for the anterior and medial direction, respectively, in the affected side. Moreover, ICCs were 0.966 and 0.965, SEMs were 1.42% and 1.78 %, and the MDDs were 3.94 % and 4.92 % for the anterior and medial direction, respectively, in contralateral side. This results show an excellent reliability of the normalised excursion distance.

Table 3-8: Normalised (% lower limb length) balance excursion of SEBT results

Side	Direction	Mean		SD	95% CI	SEM (%)	MDD (%)	ICC
		Session 1	Session 2					
Affected	Anterior (%) **	81.65	80.49	7.18	76.62-85.53	1.73	4.80	0.962*
	Medial (%)	81.10	80.59	8.96	75.28-86.39	1.53	4.24	0.981*
Contralateral	Anterior (%)	85.91	86.11	6.63	81.90-90.12	1.42	3.94	0.966*
	Medial (%)	84.56	84.81	8.04	79.70-89.67	1.78	4.92	0.965*

*Significant value P<0.05
**Percentage of lower limb length

3.5.3.2. Step test

The results of the ST show that the test-retest between-days reliability was fair with no significant relationship between the sessions ($p \geq 0.05$) for both sides. ICCs were 0.57 and 0.465 for the knee OA side and contralateral side, respectively; whereas the SEMs were 2.17 stepping for the affected side and 2.60 stepping for the contralateral side in individuals with medial knee OA. The MDDs were 6.00 stepping and 7.20 stepping for affected and contralateral sides, respectively (Table 3-9).

Table 3-9: Step test results (number of stepping in 15 second)

Side	Mean		SD	95% CI	SEM	MDC	ICC
	Session 1	Session 2					
affected	14.30	14.10	3.32	12.15-16.25	2.17	6.00	0.574*
contralateral	17.10	16.30	3.55	14.50-18.9	2.60	7.20	0.465*

*Significant value P<0.05

3.6. Discussion

3.6.1. Gait Data

The effect of lateral wedged insoles on knee pain, physical activity, and knee loading in individuals with medial knee OA will be the subject of the investigation in the main study. Therefore, to investigate the consistent of the instruments that will be used in the main study, this study was conducted. To ensure the results of the repeated gait analysis of individuals with medial knee OA at the end of the intervention are the results of the intervention itself, not the examiner error in measuring the outcomes.

The results have shown excellent between-day test-retest reliability for hip, knee and ankle angles and moments in the sagittal, coronal and transverse planes during the walking in standard shoes. However, a good test-retest reliability (CMC= 0.6) was found for foot progression; the ICC was excellent with 0.9. This may be due to the sensitivity of the foot movement to variability in the walking pattern, so the similarity between the two curves may be affected as this is in respect to the laboratory rather than a relative segment. High between-days reliability demonstrates that the markers re-application (between-days) were accurate and the errors were minimal by applying the method in section 3.4.5.3.

The majority of kinematic and kinetic parameters, in the current study, produced similar results for between-day test-retest reliability in individuals with medial knee OA. Moreover, the results of the current study were similar to most of the previous reliability studies which using a different marker set (Kadaba et al., 1989; Andrews et al., 1996; Growney et al.,1997; Tsushima et al., 2003; Birmingham et al., 2007). Between-day reliability using the Helen Hayes marker set was investigated in healthy participants in the previous studies (Kadaba et al., 1989; Andrews et al., 1996; Growney et al., 1997; Tsushima et al., 2003) except Birmingham et al., (2007) who used a modified Helen Hays marker set with 31 patients with medial knee OA. A small sample was recruited in Growney et al., (1997) and Tsushima et al., (2003), five and six participants, respectively, therefore the results cannot be generalised.

The results of the current study showed that the reliability of hip, knee, and ankle angles in the sagittal plane were excellent with the smallest SD and very low SEM and MDD compared to the angles in the frontal and transverse planes. These results agree with previous test-retest reliability reports that have evaluated healthy participants (Kadaba et al., 1989; Tsushima et al., 2003). Kadaba et al., (1989) assessed the reproducibility of hip, knee, and ankle moments and angles in the sagittal, frontal, and transverse planes in forty healthy participants (age range 18 - 40 years old) who walked

at their self-selected speed. They found that between-day reliability of hip, knee, and ankle angles and moments were excellent in the sagittal, frontal, and transverse planes and the knee angle in the frontal plane was good which is confirmed by the current study. The current results showed the between-days reliability of knee angle in the frontal plane was high (CMC=0.97) compared to Kadaba et al.,'s (1989) study (CMC=0.737), this may due to the use of a different method in the current study or the different population group. The CMC for hip, knee, ankle angles in the sagittal, frontal and transverse planes range from 0.82 to 0.99 in the current study, which supports the previous findings (Collins et al., 2009). Between-days was high with CMC ranges from 0.82 to 1.00 in older healthy participants using 6DOF marker sets for the same joints and planes (Collins et al., 2009). Moreover, the current results agree with Birmingham et al., (2007) who investigated the between-days reliability of the EKAM in thirty-one individuals with medial knee OA. In the current study, the ICC was 0.99 with 0.38% for the SEM while the ICC and SEM were 0.86 and 0.36, respectively, in Birmingham et al.,'s (2007) study. The tiny difference in the results may be explained by the instability of the markers may occurred, they used a different marker set, and the sample size was higher in Birmingham et al., (2007).

3.6.2. Dynamic Balance

Dynamic balance is affected by medial compartment knee OA and in this study, we have determined that the modified SEBT is both a reliable and more functional test of dynamic balance than the commonly used ST. Both raw and normalised excursion distance demonstrated high reliability for both sides with the anterior/medial directions with ICCs ranging from 0.92 to 0.98. However, the ST was less reliable for the affected side (knee OA) and contralateral side in individuals with medial knee OA, with ICC ranging from 0.57 to 0.46. So far, no studies have investigated the reliability of the SEBT and ST in individuals with medial knee OA, therefore this study is the first study that has compared both tests in measuring dynamic balance and evaluated the between-session reliability. However, the test-retest reliability of the original SEBT has been investigated in many studies in healthy subjects (Kinzey and Armstrong, 1998; Munro and Herrington, 2010).

The findings of this study support those of Kinzey and Armstrong (1998) who found that the test-retest reliability ranged from 0.67 to 0.87 in young healthy subjects. The participants performed five trials in four different diagonal directions; antero-medial, antero-lateral, postero-medial, and postero-lateral with wearing shoes. This procedure could reduce the consistency of the results because a variety of footwear may affect the reliability values by changing the balance base. Fatigue

is another potential reason that could occur during the trials, therefore the reach distance may be influenced significantly (Gribble et al., 2004) leading to reduce the reliability. In addition, The findings of this study support those of Plisky et al., (2006) who found that the test-retest reliability (between sessions) of the SEBT with normalised distances (to leg length) was excellent, with ICCs ranging from 0.89 to 0.93; however, only three directions (A, PM, PL) were tested with athletes subjects (Plisky et al., 2006).

Most recently, Munro and Herrington (2010) demonstrated that the between-session reliability of the SEBT was high in all eight directions. ICCs were 0.84 and 0.86 for normalised excursion in anterior and medial directions, respectively. Whereas, for the raw excursion, ICCs were 0.88 and 0.90 for the anterior and medial directions, respectively. Their findings were lower compared to the current study, and this may be explained by the current study as this used modified SEBT where very accurate lines are on the platform determining foot position accurately throughout the tests in two sessions with the block denoting the distance reached. The participants in Munro and Herrington's (2010) study were younger and healthy, therefore the different age groups and diseases may play a role as psychological reasons and may be the standard test ordering which was followed in the current study allowed for a highly consistent performance. Additionally, it may also be because the healthy individuals are reaching very far and the OA subjects are limited so the actual distance is probably lower and therefore some of the variability is reduced. However, there are slight differences in the ICC values in all the reliability studies of the SEBT (Kinzey and Armstrong, 1998; Hertel et al., 2000; Plisky et al., 2006; Munro and Herrington, 2010) including the current study, SEBT has shown excellent reliability to measure the dynamic balance in healthy subjects and in individuals with medial knee OA.

To our knowledge, this study is the first study that has investigated the reliability of ST to measure dynamic balance in individuals with medial knee OA. The current study shows that the ST has fair reliability to measure dynamic balance for both sides (ICC>0.47-0.57). Two previous studies investigated the reliability of step test to measure dynamic standing balance in stroke patients (Hill, 1996; Hong et al., 2012). Hill (1996) investigated the reliability of the ST to measure dynamic standing balance in stroke patients. Test-retest reliability was high with ICC>0.88 in stroke patients. The participants in Hill's (1996) study were stroke patients while individuals with medial knee OA were recruited in the current study, therefore the different groups could be the reason for the different ICC values. Thus, this test could be suitable for individuals with cardiovascular diseases or upper motor neuron lesion. In the majority of the knee OA studies (Hinman et al., 2002; Bennell et al., 2010), they have used the ST with a 15 cm step height (as with this study) whereas the step height

was 7.5 cm in Hill's study (1996), therefore increasing step height could reduce the reliability of the ST because the participants need stronger muscle to lift their leg higher and may lead to muscle fatigue with repetition (less muscle performance with lower height). The same reason (variability of step height and different population) could be behind the reduction in the ICC value (ICC=0.47-0.57) in the current study compared to a recent study (Hong et al., 2012). They used videotapes to record the trials (three trials) and from data of the second and third trials, ICCs were calculated (ICC=0.981-0.993) in Chinese population with stroke. Therefore, by using the data of the second and third trials, the learning effect could be reduced and thereby the ICC improved significantly.

As with any study, there are limitations to these results that include the relatively short time between tests which may have created some familiarisation effect although this should be controlled with the four practice trials for SEBT. The small sample size could be criticised although significant correlations have been found with small SEMs. Finally, the population sample were all individuals with mild knee OA and future studies should determine whether the results are applicable to greater severities of knee OA.

3.7. Conclusion

This is the first study that has investigated the reproducibility of kinematic and kinetic parameters using a rigid cluster model in individuals with medial knee OA. The EKAM was chosen to be assessed as a primary outcome in determining the effectiveness of LWIs in the pre-post intervention study and it has been demonstrated to have an excellent reliability to measure load on the medial compartment of the knee joint with a small SEM and lower minimal detectable difference. Moreover, this is the first study that has investigated the reliability of the SEBT and ST. The SEBT was shown to be more reliable tool to measure dynamic balance in subjects with medial knee OA with excellent ICCs, small SEMs with a lower minimal detectable difference and can accurately determine any improvement in balance after intervention. Therefore, from the results attained in this study, the Star Excursion Balance Test will be used in the planned study to assess dynamic balance in in individuals with knee OA.

Chapter Four

The effectiveness of a lateral Wedge insole on osteoarthritis Pain, activity level and joint Loading (WPAL study)

4.1. Introduction

The medial compartment of the knee joint is ten times more frequently affected than the lateral compartment (Ledingham et al., 1993) because it may exposed to a 2.5 times greater load than the lateral compartment during gait and the line of the ground reaction force (GRF) passes medially to the medial compartment of the knee joint (Schipplein and Andriacchi, 1991; Hinman et al., 2013). This results in increased loads on the knee joint across the medial compartment of the knee joint, as measured by the external knee adduction moment (EKAM), which is a surrogate measure of medial knee load during ambulation (Schipplein and Andriacchi, 1991) during gait analysis (Hinman et al., 2013). Individuals with knee OA have a higher EKAM compared to healthy subjects and thereby an increased load on the knee joint (Schipplein and Andriacchi, 1991). The relative risk of presence and progression of medial knee OA is associated with increased loading on the medial knee joint during gait (Miyazaki et al., 2002; Andriacchi and Mündermann, 2006) and disease severity is increased with a higher EKAM (Sharma et al., 1998; Hurwitz et al., 2002; Thorp et al., 2006; Landry et al., 2007; Huang et al., 2008; Bennell et al., 2011b).

Reducing the load at the knee is suggested to be an attractive option to treat medial knee OA. One such treatment, lateral-wedge insoles which are considered as a conservative (non-pharmacology) intervention in individuals with knee osteoarthritis (Jordan et al., 2003; Bennell and Hinman, 2005; Zhang et al., 2010). They are a low-cost intervention, simple to use, and are used to reduce the EKAM by shifting the ground reaction force laterally, and thereby decreasing the moment arm which results in a reduced the EKAM on the knee joint (Kakihana et al., 2005; Baker et al., 2007), and thereby potentially reduce the progression of knee OA (Miyazaki et al., 2002). Whilst LWI decreased the EKAM in individuals with medial knee OA (Barrios et al., 2013), studies have shown that lateral wedge insoles (when compared to a neutral insole) do not reduce pain level (Pham et al., 2004; Baker et al., 2007; Bennell et al., 2011b; Parkers et al., 2013). However, while pain level is of utmost importance, the overall activity level of the individual may have changed which may have resulted in more activity with the individual walking to their pain level. Therefore, physical activity

level should be measured with lateral wedged insoles alongside pain. Measuring all parameters of level of physical activity (duration, frequency, and type/intensity) within a specified timeframe, level of physical activity measured in all daily life, and a measure of joint loading for each reported activity are recommended for the collection of physical activity data by a recent study (Gates et al., 2017).

The reduction in level of physical activity is mainly due to increased knee pain and the fear of falling during the physical activity (McAlindon et al., 1992; Fitzgerald et al., 2004). Dunlop et al., (2011) found that pain and function were associated with the level of physical activity in knee OA. Moreover, reduction in activity level is the main characteristic of patients with knee OA in addition to sedentary time (time spent in sitting and lying position) increases in individuals with knee OA (Dunlop et al., 2011). The number of steps was shown to have decreased in knee OA patients compared to healthy subjects and they also needed to stop whilst walking due to knee pain (Mitsui et al., 2008; Tudor-Locke et al., 2011c; White et al., 2014). In addition, reducing the level of activity is associated with the majority of health problems such as obesity, heart disease, diabetes, and hypertension (Pedersen et al., 2006). Duvivier et al., (2013) found that reducing inactivity by increasing the time spent walking or standing is more effective than one hour of physical exercise. In addition, a recent study suggested that limiting sedentary behaviour by reducing sedentary time and improving physical activity in individuals with knee OA might be important in maintaining their function over the time (Semanik et al., 2015).

As mentioned in chapter two, self-report questionnaires are unreliable and cannot accurately determine sedentary behaviours (Washburn and Montoya, 1986) while pedometers cannot measure quiet standing and are less accurate in measuring slow walking (Kinnunen et al., 2011). Alternatively, the activPAL3 monitor can distinguish between changes in these positions (Figure 4-1), measures time spent sitting/lying, standing/stepping, and cadence (Dahlgren et al., 2010), and walking length. This monitor has been validated to measure static and dynamic activity in adults (Godfrey et al., 2007). The activPAL3 monitor is more valid and accurate to measure sedentary behaviour in older population compared to Actigraph (Lyen et al., 2012) and it is better and more valid to measure slow walking than the Actigraph and pedometer.

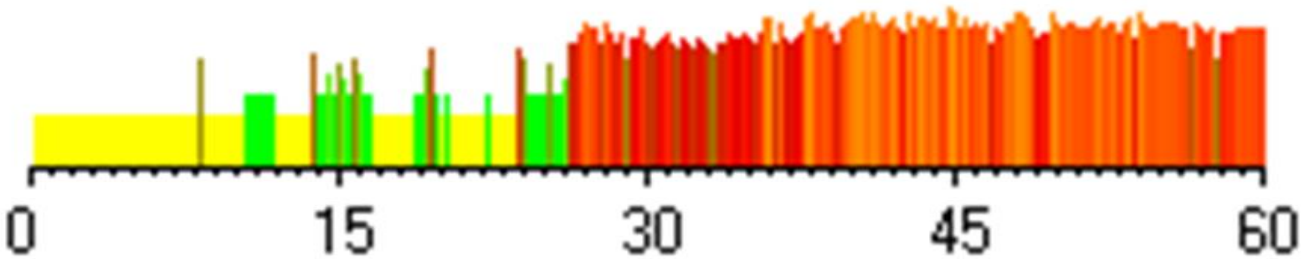


Figure 4-1: ActivPAL3 (initial data); Yellow=sitting, Green=standing, Red=stepping in 60 minutes.

In addition, there was a strong correlation between the activPAL3 and video observation for slow walking, time spent in sedentary position, standing, and walking (Grant et al., 2008). The activPAL3 monitor is more sensitive to reductions in sitting time than the Actigraph and it is recommended to measure sedentary time in inactive, overweight, and old adults (Kozey-Keadle et al., 2011; Lyden et al., 2012). Therefore, we propose that activPAL3 is an appropriate instrument to measure the level of activity of individuals with knee OA (Godfrey et al., 2007; Aminian and Hinckson, 2012) to measure amount of time spent in sitting/lying, standing, and walking in addition to number of steps and cadence will be measured by an activPAL3 monitor (Dahlgren et al., 2010).

In summary, evidence has shown that the external knee adduction moment is reduced significantly when using lateral-wedge insoles, however, pain and physical function do not improve significantly (Radzimski et al., 2012; Parkes et al., 2013; Hinman et al., 2013). However, it is not known if a change in the activity level of the individual is seen with lateral wedges which may counteract the reduction in symptoms that the individual is experiencing when on treatment. No study has investigated the effect of lateral-wedge insoles on activity level using an activity monitor and whether a relationship exists between pain, activity level and joint loading in individuals with medial knee OA. Additionally, there is no study that has investigated pain, EKAM and level of activity in individuals with knee osteoarthritis in one complete study demonstrating novelty an important area of clinic research. Therefore, this study aimed to determine any change in pain, EKAM, and level of physical activity when using lateral-wedge insoles, compared to neutral non-wedged insoles. The results of this study will help us to further understand the clinical and biomechanical effects of a lateral wedge insole as an efficient treatment for early stage OA.

4.2. Objectives of the study

The following will help us to understand the effect of lateral wedged insole on knee loading, level of physical activity, and knee pain. Secondly, they will allow us to determine if lateral wedged insoles are an efficient intervention for patients with medial knee OA.

4.3. Aims and Hypotheses

The primary aims are to determine whether a lateral wedged insole improves physical activity in individuals with medial knee OA and whether this improvement concurrent with reductions of the knee loading. Five hypotheses will be tested in this thesis:

1. To determine any reduction in knee load with using lateral wedged insole in comparison to the comparator group.

- Null hypothesis, There will be no significant reduction in the external knee adduction moment in the group using the lateral wedged insole compared to the comparator group.

2. To determine if there is any change in activity level due to using the lateral wedged insole compared to the comparator group.

- Null hypothesis, There will be no significant difference in level of physical activity in the group using the lateral wedged insole compared to the comparator group.

3. To determine any change in pain and function after wearing lateral wedged insole in comparison to the comparator group.

- Null hypothesis H2, There will be no significant difference in knee pain and function in the group using the lateral wedged insole compared to the comparator group.

4. To determine any change in cumulative knee loading in the group using the lateral wedged insole compared to the comparator group.

- Null hypothesis, There will be no significant difference in cumulative knee loading in the group using the lateral wedged insole compared to the comparator group.

5. To determine any improvement in dynamic balance after using lateral wedged insole in comparison to the comparator group.

- Null hypothesis, There will be no significant difference in dynamic balance in the group using the lateral wedged insole compared to the comparator group.

Moreover, this study will help to identify the following:

- Whether the physical activity will be recommended to measure objectively as a primary measurement alongside knee pain in knee OA research studies.

4.4. Method

4.4.1. Research Environment

The gait analysis work was completed at the University of Salford Gait Laboratory who have a strong record in musculoskeletal research and clinical gait analysis. The gait laboratory is situated in the Directorate of Podiatry, Allerton Building, and University of Salford.

4.4.2. Participants

Participants with an age range of 40-85 (upper age limit due to the amount of walking involved in the study) and have been diagnosis with symptomatic medial knee osteoarthritis were recruited in this study. The participants had to meet the following inclusion criteria to be eligible for the study.

4.4.3. Inclusion criteria:

To define medial knee OA, a participant must have met all of the following; their ages between 40-85 years where upper age limit due to the amount of walking involved in the study. If they complain of Pain with walking (using KOOS question), they need to have at least mild pain walking on a flat surface - clinical diagnosis by qualified clinician. If the participants have been diagnosed with mild-moderate medial knee OA by GP based on the clinical and radiographic criteria, using Kellgren and Lawrence scale (K/L) (Kellgren and Lawrance, 1975), and according to the criteria of the American College of Rheumatology (ACR) (Altman et al., 1986). These were chosen because of they need for effective symptoms relief and to delay the need for surgery as long as possible. They need to have definite medial narrowing and not lateral narrowing and evidence (osteophyte) of OA. Based on recommendations from previous studies (Childs et al., 2004; Clarke et al., 2004) and because neither

of K/L grades 0 and 1 exhibit definite joint narrowing (Felson et al., 1995; Guccione et al., 1990). In addition, the Kellgren and Lawrence grade 2 or 3 with medial narrowing are chosen as they are considered as mild and moderate radiographic knee OA (Thorp et al., 2006). Therefore, for a patient to be eligible on x-ray they must fulfil the following criteria; K/L grade 2 or 3 in the tibiofemoral joint (TFJ), the K/L grade in the TFJ must be higher than the PFJ and cannot be equal, and the medial joint space narrowing score must be higher that the lateral joint space narrowing score and cannot be equal. In addition, if they complain of medial tenderness either by their own indication that this is where they have pain or by examination showing tenderness at the medial TF joint line – Clinical diagnosis by qualified clinician. Absence of PF tenderness on examination. They are able to walk for 100 meters non-stop - participant response, speak and understand English to read the information sheet and sign consent form and they can walk without any walk assistive.

4.4.4. Exclusion criteria:

Participants were be excluded if the pain is more localized to the patellofemoral joint on examination than medial joint line, have tricompartmental knee osteoarthritis or have grade 4 medial tibiofemoral osteoarthritis on the Kellgren Lawrence scale. Other exclusions include a history of high tibial osteotomy or other realignment surgery or total knee replacement on the affected side. In addition, a history of Knee Arthroscopy with the last 6 months, Intra-articular injection into the treatment knee in the last 3 months, any foot and ankle problems that will contraindicate the use of the footwear load modifying interventions, or inflammatory arthritis including Rheumatoid Arthritis. If the participants complain of complex pain conditions such as Diabetic Neuropathic pain, fibromyalgia. The participants were excluded if they have severe coexisting medical morbidities, or currently use, or have used, orthoses of any description prescribed by a Podiatrist or Orthotist within the last 2 months. If the participants cannot understand procedures, unable to walk unaided and have to rely on a stick, crutch or frame, or cannot walk for 100 meters without stopping they were also be excluded, as they may be unable to complete the full testing protocol.

A clinical exam was performed by the examiner for all participants to confirm they had medial knee OA that included palpation of the medial aspect of the knee.

4.4.5. Sample size

Twenty participants with medial knee OA were recruited in the experiment. These 20 participants were randomly assigned into an intervention group (LWI) and comparator group (neutral insoles), 10 subjects for each group. As no study has been undertaken before on activity monitoring in medial knee OA with the use of interventions, the sample size has been decided pragmatically and will be used to determine an appropriate sample size in future large-scale randomised clinical studies.

4.4.6. Recruitment

Ethical approval was obtained from Salford University (HSCR14/24) and the recruitment of participants was from two sources; The University of Salford holds a register of individuals who have responded to a call in regards to being diagnosed with medial knee osteoarthritis. In addition, individuals from the local community who have been diagnosed with OA inside their knee. An invite letters were sent with pre-paid envelopes to each of all potential participants who were interested to take part in the study with the participant information sheet (PIS). Afterwards, the investigator contacted the participant who did not respond or who responded but needed more explanation for any further information in nature and requirements of the study. Only once the patient has had time to read the Participant Information Sheet (PIS) and eligibility confirmed, gait lab appointment was booked. (Figure 4-2)

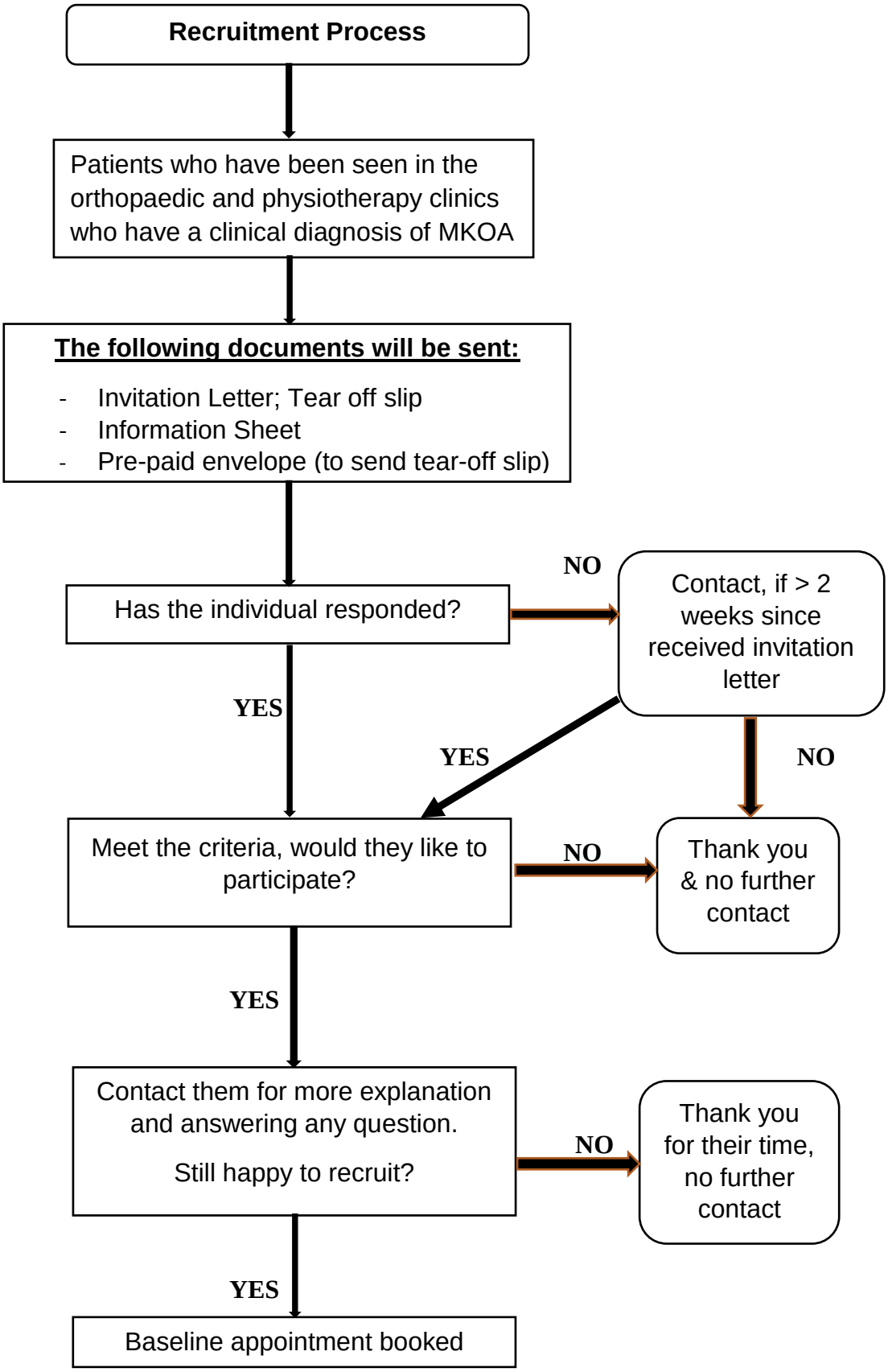


Figure 4-2: Recruitment chart flow.

4.5. Study design and procedures

This study is aiming to understand the effect of lateral wedge insoles in comparison to neutral (non-wedged) insoles. The randomisation slips were generated before the visits and the order of treatment (lateral wedged and neutral insoles) was determined from these randomisations. The study was performed in two different groups, group A is the intervention (LWI) group and group B is the comparator group. To examine the effect of both insoles and compared between them, pre-post intervention (parallel) study design has been used in the study involving four visits to the gait laboratory with a six-week intervention period as detailed in Figure 4-3. In addition, this study is a part of PhD and limited time was available to conduct this study, therefore parallel study design was chosen. In addition, parallel study design is commonly used to compare between active treatments vs. placebo with no carry-over effect that may be experienced with other designs (i.e. cross-over study). The current study was conducted for six weeks to examine the effect of LWI after six weeks and during the intervention (week one) to determine any change biomechanical and clinical changes and then compared the findings with comparator group and baseline. In addition, a cross-over trial was undertaken for six weeks by Baker et al., (2007), therefore six weeks was reasonable period and allowed comparison to the Baker et al., (2007) study.

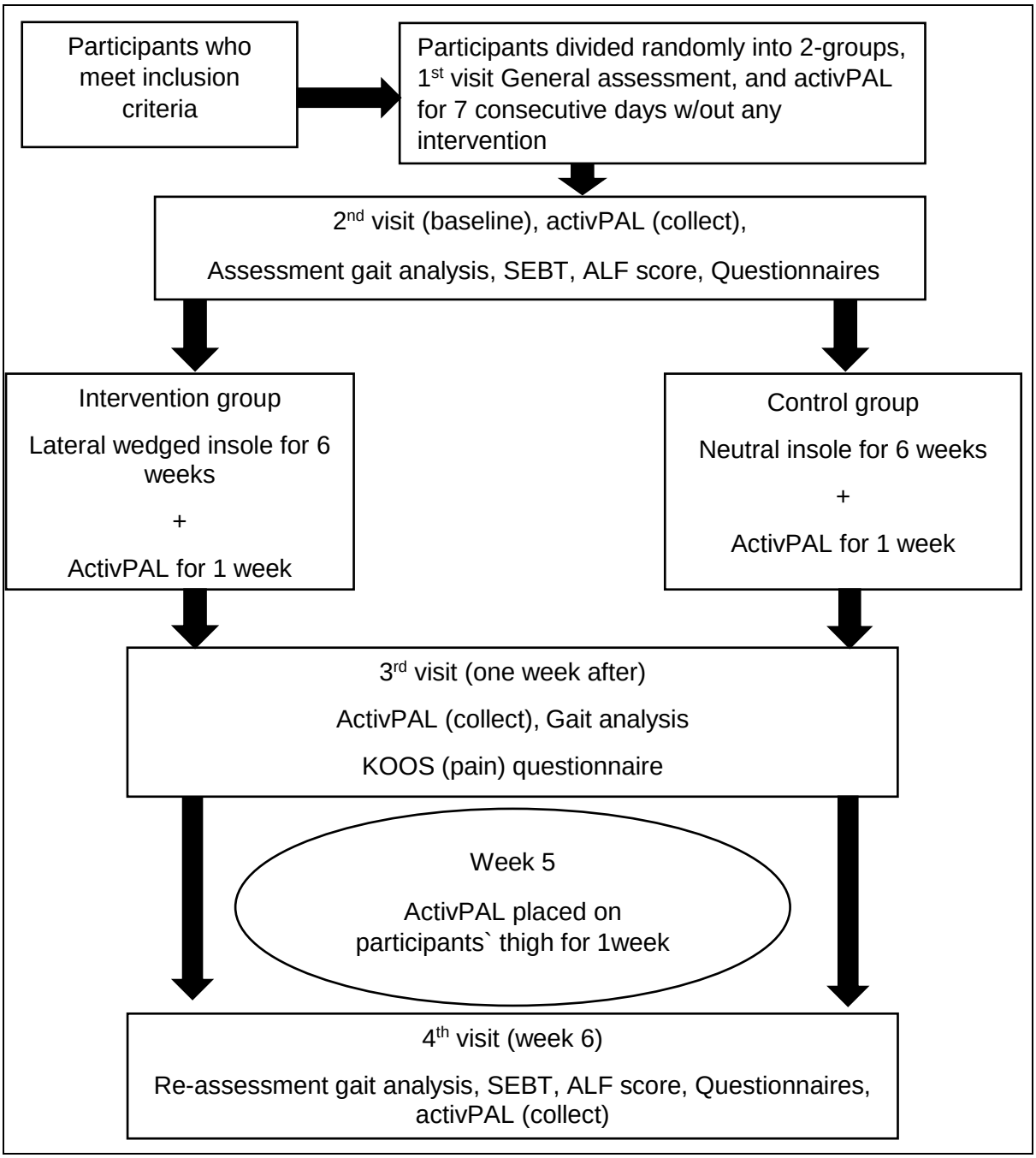


Figure 4-3: Block diagram of study protocol.

The function of each activPAL3 device was tested by the investigator on himself before use the device in the study to check whether the device would work appropriately and collect the activity data. This procedure consisted of the following tests:

(i) The activPAL3 monitor collected data and distinguished the different activities such as spent time (in sitting, standing, stepping), cumulative of steps, and number of steps at a

specific time and the outcomes of the monitor compared with stopwatch and direct observation.

The main investigator performed all the tasks for control and determine time (Table 4-1) at Mary Seacole laboratory, University of Salford after he fixed the device (activPAL3) on his anterior medial aspect thigh by adhesive tape. The collected data was analysed by the main investigator and showed that the activPAL3 identified all the tasks correctly. This procedure was repeated once for each device to test if the activPAL3 monitor work properly.

Table 4-1: Five tasks that performed to test the correct function of each activPAL3

Task	Time	steps
Normal walking	For five minutes	counted by the investigator
Slow walking	For one minute	counted by the investigator
Backward walking	For one minute	counted by the investigator
Standing position	For one minute	counted by the investigator
Sitting position	For one minute	counted by the investigator

(ii) To check whether the devices are working properly (immediately before placed on their high);

In this part, the device was placed on a table in two positions (vertical and horizontal) for one minute for each position. To ensure the activPAL3 work properly and discovered the changing between the positions. This procedure was performed for all the devices before placing them on the participants` thigh.

Visit one "Pre-baseline"

Upon arrival at the gait laboratory, the study was explained in full and if the participants were happy, they completed and signed the consent form after asking any questions they may still have had. Following this, they were asked to wear the activPAL3 for continuously for seven consecutive days for 24 hours. The device was secured to their upper leg with double-sided hydro gel adhesive pads (PALstickies, hypo-allergenic) and covered by waterproof adhesive tape. This was worn throughout the day included bath/ shower or swimming. An activPAL3 was used because it is valid to measure slow walking and more sensitive for slow speed reduction compared to Actigraph (Ryan et al., 2006;

Dowd et al., 2012) and more accurate to measure low intensity activity than Pedometer (Mathie et al., 2004). It is more valid to measure sedentary behaviour for old, inactive, and overweight population than Actigraph monitor (Kozey-Keadle et al., 2011). In addition, this duration (seven days) has had chosen to gain a valid data (Godfrey et al., 2007; Maddocks et al., 2010), captured the data during weekend and weekdays, and to help us to gain information about their physical activity level before using any of the insoles. The diary was given to complete during the following week to know wearing time, adherence of the participants, and if they did any unusual activity to them or unexpected factors that could stop them to wear the device or doing their activity (Appendix 3). Following this visit, the participants asked to attend to the University of Salford after one week to complete the assessment (baseline for other outcomes) and collected the device.

Visit two "Baseline"

One week after visit one; the participants attended the Salford University gait laboratory. The diary log was collected. The activity data was downloaded to a personal PC and re-programmed to collect activity data for one week. Following this, they were asked to change into shorts and a comfortable T-shirt and demographical measurements were undertaken; height, mass, and leg length (to normalized outcomes of SEBT to leg length). They were then instructed to complete the four questionnaires in regards their knee pain and activity.

Questionnaires:

Knee injury and Osteoarthritis Outcome Score (KOOS); it holds 42 items in symptoms (7 items), pain (9 items), activity of daily living (17 items), sport and recreation (5 items), finally, knee-related quality of life (QoL) (five items). All items have five possible answer scores from (0) to (4). This questionnaire takes about 10 minutes to complete and the last week is the time-period considered when answering the questionnaire (Roos et al., 1999). The total score of each subscale was calculated and normalised (using the KOOS software; http://www.koos.nu/) from (100) indicates no problems to (0) indicated extreme problems.

Physical Activity Scale for the Elderly (PASE); a self-reported questionnaire (PASE) was used to assess of physical activity in the elderly during a one-week period of time. It is reliable, valid and sensitive to change in individuals with knee OA (Washburn and Ficker, 1999; Martin et al., 1999). PASE assesses time spent in walking outdoor, sport, and recreational. In addition, participants were

assessed in housework, home repairs, and work for pay or as volunteer and outdoor activities such as gardening. PASE asks about frequently and duration of these activity.

Intermittent and Constant Osteoarthritis Pain (ICOAP); Knee Version. The ICOAP is the first questionnaire to consider intermittent and constant knee pain reported by patients which asking about the pain that last it in the previous week (Liu et al., 2014). The ICOAP is divided in two subscales with 11 items and covers different aspects; psychology, intensity "(0) not at all to (4) extremely" and frequently "(0) never to (4) very often" of that pain. A five items for constant knee pain and a six items for intermittent knee pain. Each item is scoring from 0 to 4 according to the order they appear in the questionnaire. The ICOAP is reliable and valid to measure the knee osteoarthritis pain (Gonçalves et al., 2010; Bond et al., 2012). Test-retest reliability was excellent (ICC 0.85) in subjects with hip and knee osteoarthritis, aged 40 years and older and there was a significant correlation between ICOAP and each of the other questionnaires (WOMAC & KOOS) (Hawker et al., 2008; Bond et al, 2012).

12-item Short Form Health Survey (SF-12); is a shorter version of SF-36 that provides a physical component scale (PCS) and mental component scale (MCS). This questionnaire comprises 12 questions measuring the following: bodily pain, general health, mental health, physical functioning, social functioning, role limitation due to physical and emotional health, and vitality. It is valid and reliable (>0.73) to determine the health-based Quality of Life (QoL) and takes two minutes to complete (Ware et al., 1998).

Following this, they were asked to perform the star excursion balance test to assess their dynamic balance. The procedure of this test has been mentioned in chapter three (3.4.4.1). Then, Aggregated Locomotor Function (ALF) score was performed where three functional tasks; (walk eight metres, ascend and descend seven stairs, and transfer from a sitting to standing position) were undertaken to test their physical function. These three task are recommended and used to evaluate the three common tasks with individuals with knee OA ((McCarthy et al., 2004). Each task performed separately with one-minute break in between to avoid any potential fatigue and time in second was recorded. This allowed the calculation of ALF score.

The next step, gait data was collect according to the following:

Gait Analysis; System calibration (L and T shaped) was performed, before the participant comes in, by investigator to confirm the accuracy of kinetics gait and to determine the position and orientation of the cameras relative to the laboratory coordinate system. Small reflective markers was attached on bony landmarks using hypo-allergenic adhesive tape. Individual markers was attached on anterior superior iliac spines (ASISs), posterior superior iliac spines (PSISs), iliac crests, right greater trochanter, left trochanter, lateral femoral epicondyles, medial femoral epicondyles, lateral malleoli, medial malleoli, the 1st, 2nd and 5th metatarsal heads and Calcaneal tubercle, In addition, cluster pad with four markers was fixed to the shank, thigh, and pelvis using Fabiofoam Superwrap bandages. A static trial, where the participant stood on a force platform for 10 second, was obtained from the 16 cameras. All markers must be identified by the cameras and then these markers were removed leaving only the cluster plates on the shank, thigh and pelvis (tracking markers). The participant was instructed to walk 10 times throughout the walkway at self-selected walking speed with the following conditions; shod only, and with the 5-degree lateral wedge insole or with a neutral insole. Five successful trials (the participant`s foot must be strike the force platform, complete stance by one foot within one force platform) were analysed. At the end of this visit, an insole was inserted into their own shoe and asked to wear for a minimum of (6) hours per day for six weeks during daily activity with activPAL3 monitor for other one week (seven consecutive days). The diary questionnaire was given to complete during the following week.

Visit three "follow-up 1"

The 3rd visit was conducted one week after the second visit. The activPAL3 device was collected in this session to analyse participants' activities during the previous week. Height, mass was measured. Once the markers were attached, two conditions were tested; 1. Their own shoe 2. Their shoe with insoles (5˚ lateral wedged insoles or neutral insoles) and then stand on one force platform for 10 seconds for static image and gait analysis was undertaken same as visit two. Their shoe must be the same shoe at baseline to ensure that any change in the EKAM was not due to differences in shoes. They then completed the KOOS questionnaire in regards to their pain. At the end of this visit, an insole was inserted into their own shoe and asked to wear for a minimum of (6) hours per day for six weeks during daily activity. ActiviPAL3 was not given to the participants in this visit.

At week 5, an activPAL3 was placed on their thigh for one week (seven consecutive days) and the diary log was given for the following week (the device either sent by post or home visit was arranged).

Visit four "follow-up 2"

The fourth visit conducted six weeks after the second session (baseline). The same procedures as the second visit were undertaken. The diary and activPAL3 were collected from the participants.

4.6. Outcome measures

These following outcome measures enabled us to test the hypotheses concerning the effect of the insoles on pain, activity, and knee loading in individual with medial knee OA.

4.6.1. Primary outcome measure

4.6.1.1. External knee adduction moment (EKAM)

Kinematics and kinetics data were measured during walking for all trials using a 16 camera Qualisys (Qualisys, Sweden) motion analysis system operating at 100 Hz and four force plates (AMTI, USA) operating at 1000 Hz.

The first peak of EKAM is measured commonly in majority of the studies with the knee adduction angular impulse (KAAI) in individuals with knee OA (Hinman et al., 2013; Jones et al., 2014). The KAAI is more sensitive to measure of load on knee joint in mild-moderate knee OA, it considers the magnitude and duration of the load on the knee joint (the area under the adduction curve) (Thorpe et al., 2006). The first peak of EKAM was normalized to body mass (Nm/kg) whereas, the KAAI normalized to body and stance time (Nm/kg.s). The change in the EKAM and KAAI were recorded in time points (baseline, immediately effect, week one, week six) for both groups. The results help us to determine the change the EKAM over time points in LWI group compared to baseline and compared to comparator group.

4.6.1.2. Level of physical activity:

The activPAL3 monitor was collected at visit two (baseline), visit three, and visit four (week 6). The activPAL3 uses the inclination of the thigh to classify posture (thigh in horizontal position, detects

sedentary behaviour; vertical position, detects upright, when an upright position is detected the acceleration signal to detect cyclical stepping movement which classified as walking). The activPAL3 data downloaded to the personal computer via a USB interface for analyses with activPAL3 software (PAL Technologies Ltd. V 7.2.28) and exported into Excel (Microsoft Corporation, Microsoft Excel 2010) for more analyses (Griffin et al., 2011). Only days on which the participants wore the monitor for at last six consecutive days and 12 hours a day were analysed. The data which did not meet these criteria were excluded. To calculate volume of the activity per a day, the data file which was downloaded from activPAL3 to the computer was opened through activPAL3 software and then saved as summary results under specific name which indicate to specific day. The mean of number of steps, time spent in sitting, standing, and walking was calculated for all participants to determine any change in each group after one week of wearing insoles and six weeks compare to baseline and compared to the other group. Walking pattern as well as cadence were analysed and calculated to determine any change in both groups (see section 4.9). The results of these methods helped us to look depth in their activity and find out whether individuals in LWI group changed their activity compared to comparator group.

4.6.1.3. Pain level:

Pain level was evaluated by the KOOS scale holds (9) items and all items have five possible answer scores from (0) no pain to (4) extreme pain. The total score of each subscale was calculated and normalised (using the KOOS software, http://www.koos.nu/) from 100 indicates no problems to 0 indicated extreme problems. The pain level was assessed using KOOS in baseline, week one and week six of trials to determine any difference between lateral wedge group and comparator group and time point.

4.6.2. Secondary outcome measures

4.6.2.1. Dynamic balance using Star Excursion Balance Test

Star Excursion Balance Test (SEBT) measures maximal distance that will be reached by using one leg in different directions, and then return slowly to starting position (double support) with keeping balance throughout the test (Olmsted et al., 2002; Gribble et al., 2007). The directions relative to the support leg on the platform. Anterior (A), medial (M) directions are the most relevant to knee OA condition. Because quadriceps muscle strength and gluteus medius muscle strength are decreased in knee OA (Slemenda et al,. 1997; Sled et al., 2010). Participants performed this test seven times (four

times practice and three times as a test) for each direction (anterior and medial). The reach distance was recorded in centimetres and both raw data and normalised data (to lower leg length) were analysed. Normalized excursion distance = (excursion distance/leg length)*100. The average of three test trials was calculated for all data, two directions, and both groups.

4.6.2.2. Knee injury and Osteoarthritis Outcome Score (KOOS) other items

KOOS other subscales hold 33 items in symptoms, activity of daily living, sport and recreation, and QoL. All items have five possible answer scores from (0) no problem to (4) extreme problem. The total score of each subscale is calculated and normalised (using the KOOS software; http://www.koos.nu/) from 100 indicates no problems to 0 indicated extreme problems. This was assessed at baseline, and at the week 6 period to identify any differences between groups or within group.

4.6.2.3. Physical Activity Score for the Elderly (PASE)

A self-reported questionnaire (PASE) was used to assess of physical activity in the elderly during the previous 7 days period. The total PASE score = (time spent in each activity (hour/ week) or participation (yes/no) × PASE weight. The overall score ranges from 0 to 400 where high score indicates high physical activity. Scoring software is provide in the PASE administration at http://www.neriscience.com/

The PASE was assessed at baseline, and week 6 for both groups to identify any differences between groups or within group.

4.6.2.4. Aggregated Locomotor Function (ALF) score

The ALF score is a total of the mean time of three locomotor tasks in seconds. Each task was performed (three time) separately with one-minute break in between at baseline and week six for all participant in both groups.

4.6.2.5. 12-item Short-Form Health Survey (SF-12)

The SF-12 provides a physical component scale (PCS) and mental component scale (MCS) and will be scored using QualityMetric Health Scoring Software version 2, (http://www.qualitymetric.com/demos/TP_Launch.aspx?SID=52304).

The general scaring between 13-69 for PCS and 10-70 for MCS, a high score represents a good health-related QoL. This questionnaire was assessed at baseline, and week six to determine any change after using lateral wedged insoles for six week compared to baseline and comparator group.

4.6.2.6. Intermittent and Constant Osteoarthritis Pain (ICOAP)

The ICOAP is divided in two subscales with five items for constant knee pain and a six items for intermittent knee pain. Each item is scoring from (0) no pain to (4) extreme pain according to the order they appear in the questionnaire. Constant knee pain consists of five items and score ranges from 0-20, intermittent knee pain subscale consists of 6 items and score ranges from 0-24, total pain score ranges from 0-44. A total score was calculated and normalized from (0) no pain to (100) extreme pain. For total pain score, using the following formula: (Total pain score / 44) x 100. ICOP was assessed in baseline and week six to determine any difference between lateral wedge group and comparator group or time point.

4.6.2.7. Cumulative knee loading

Cumulative knee load is a biomechanical approach that measures of abnormal loading on tibiofemoral joint during physical activity (Maly, 2008). Cumulative loading measures the total exposure to joint loading during physical activity by measuring the mean of knee adduction moment impulse of the five walking trials using three-dimensional gait analysis multiplied by one half of the mean number of steps/day taken by one leg using accelerometer (activPAL3). The individuals with knee OA produce higher CKL regardless of a lower step count because the load on the knee joint still high, two times greater than healthy individuals (Maly et al., 2013).

CKL was measured to assess excessive and repetitive load during free live activity and to determine any change in the cumulative knee load (CKL) in participants with knee OA after the intervention by measuring normalized knee adduction moment impulse during walking at self-selected walking speed and daily number of steps. To calculate the CKL in the current study, average of the five trials of the KAAI was multiplied by one half of the mean number of daily steps (Robbins et al., 2009).

The activPAL3 measured the total steps by both legs, therefore total number pf steps divided by two. The CKL is normalized to body mass (KNm/kg*s).

4.7. Treatments

A pair of off-the shelf lateral wedged insoles (SalfordInsole™) with a 5 degree inclination at the heel (as greater wedging is associated with foot discomfort) (Kerrigan et al., 2002) (Figure 4-4) were utilised in this study. To reduced foot and ankle associated pain, the inclination gradually reduced to 0 at the 5th metatarsal head (Jones et al., 2013b & 2014). These insoles used in this study are developed at the University of Salford and made from a comfortable and flexible material (SureStep-Control™, with a medium Shore values A 70 which is similar to high material density). 5˚ LWIs are full length lateral wedged insoles with a medial arch for supporting and they have been used in the current studies to reduce medial knee loading and knee pain (Jones et al., 2013b & 2014). The neutral insole has a flat surface with no inclination (Figure 4-4) was worn for the comparator group (control condition). The depth and density of both insoles are identical (4mm and Shore A 70). Both insoles were placed within participants own shoe to make the method of the trial more applicable and this procedure was recommended by Lewinson et al., (2016).

a b

Figure 4-4: (a) Neutral insole, (b) 5˚ Lateral wedged insoles.

4.8. Randomisation, concealment and blinding

It was not possible for the investigator to be blinded to the condition where the current study is a part of PhD study. The participants were presented both neutral insoles and wedge insoles as active treatment thereby not knowing which the active treatment is. Therefore, we would characterise this trial as single blind.

4.9. Data analysis

The kinematics data were recorded during stance and swing phases (normalized to gait cycle) whereas kinetics were recorded during stance phase (normalized to stance phase). The average of the maximum and minimum of all trials for kinetics and kinematics were analysed for each condition and each visit in excel files for each. In addition, ROMs were calculated from the differences between the maximum and minimum values of kinematic data. The curves of the kinematic data in sagittal plane were divided into maximum flexion (1%-33), minimum flexion (34%-67%), and maximum flexion (68%-101%) for sagittal hip angles. The curves of the kinematic data in sagittal plane were divided into initial contact, loading response (2%-21), mid-stance (22%-51%), terminal stance (52%-62), and mid-swing (63%-101%) for sagittal knee angles. The curves of the kinematic data in sagittal plane were divided into initial contact, loading response (2%-21), maximum dorsiflexion (22%-101%), and minimum dorsiflexion (22%-101%) for sagittal ankle angles. The graph of vertical ground reaction (GRFv) forces were divided in three sub-phases which are early stance peak (1%-33), trough or mid-stance (34%-67%), late stance peak (68%-101%). The average of the means of spatio-temporal variables for each visit, condition and for each group were analysed.

For physical activity, the data from activPAL3 monitor was downloaded and activity files were processed in excel to obtain a total standing time, total stepping time, total sedentary time, and total number of steps for seven days for each participant in both groups and for each visit, that data is considered as overall volume of activity. The average of the seven days was calculated for all parameters and all participants. To examine the pattern of walking, the length of all walking events and cadence of these walking events were calculated. The activity data for each participant were opened through activPAL3 software and saved as "save event data" (.csv files). These files were processed in Matlab to extract all walking events, a continuous period of walking. These walking events were put into bins (bands) of walking event length (0-0.5 min, 0.5-1 min, 1-2 min, 2-3 min, 3-4 min, 4-5 min, 5-10 min, 10-20 min, 20-30 min, >30 min) and all durations in each bin were summed. An average for each bin was calculated by dividing this total by the number of participants

and the number days. Cadence (intensity of walking) for each walking event was calculated by dividing the number of steps in the walking events by the duration of the walking event. These walking events were put into bins (bands) of cadence value (≤10 steps/min, 10-20 steps/min, 20-30 steps/min, 30-40 steps/min, 40-50 steps/min, 50-60 steps/min, 60-70 steps/min, 70-80 steps/min, 80-90 steps/min, 90-100 steps/min, 100-110 steps/min, 110-120 steps/min, 120-130 steps/min, 130-140 steps/min, 140-150 steps/min, 150-160 steps/min, 160-170 steps/min, 170-180 steps/min) and all duration in each bin were summed. An average for each bin was calculated by dividing this total by the number of participants and the number days. For other parameters, the average of excursion distance of balance data, questionnaires, and three tasks of ALF test were calculated for each participant in all visit for both groups.

Statistical analysis was performed using SPSS and Excel (version 11.5). The normality of all variables checked by using the Shaprio-Wilk test to determine whether the distribution of the data was normal ($p>0.05$) or not ($p<0.05$). In this study, there were two independent factors where one factor is between-groups (intervention and control) which was tested one dependent factor (i.e. EKAM) at three different time points (within-group), therefore mixed ANOVA, compares the mean differences between and within groups, was performed for all variables to determine which treatment was more effective. Independent t-test was performed to compare between groups if there was interaction between the two independent factors to determine where the difference is lie. Descriptive data for all data were calculated for all variables of kinetic, kinematic, physical activity, questionnaires, and balance data.

The majority of the data were parametric data and the rest of the other data that were non-parametric were not highly deviated. A mixed ANOVA test was used in this study because his test is not significantly sensitive to moderate deviations from normality (Glass et al., 1972, Harwell et al., 1992, Lix et al., 1996; Ghasemi & Zahediasl, 2012). In addition, Importantly, because the design of this study were there are two different treatment groups which were assessed at three different point times (pre-treatment, during treatment, and post-treatment), A mixed ANOVA with applying Bonferroni correction (to reduce type 1 error) was used. To find out the effectiveness of LWIs on knee loading compare to baseline and comparator insoles, mixed ANOVA tests were conducted and the level of significance for all statistical tests was set at an alpha level of 0.05.

4.10. Results

The following is the presentation of the results for the study when comparing the lateral wedged insole group to the neutral insole group. The results are structured so that the primary outcome measures are explained first and then the secondary outcome measures.

4.10.1. Participants

Twenty patients with confirmed painful medial knee osteoarthritis (KL grade 2/3) were recruited to participate in this study (19 male, 1 female). They were randomly assigned into two separate groups, ten participants for each. Their ages range was 47-78 years and 47-73 years; heights range 161-191 cm and 162-183 cm; mass range 51-110 Kg and 62-108 Kg; body mass index (BMI) rage 20.2-32.9 Kg/m² and 22-34.7 Kg/m² for neutral insoles group and lateral wedged insoles group, respectively. There were no significant differences between the groups in term of these variables ($p \geq 0.05$). (Table 4-2)

Table 4-2: Baseline demographic data of both groups.

	Neutral Insoles* (n=10)	Lateral wedged insoles (n=10)	P-value
Age (mean years ±SD)	62.4 ±10.4	60 ±9.2	0.59
Height (mean cm ±SD)	174.8 ±9.4	174.7 ±7.4	0.97
Mass (mean Kg)	82.5 ±21.6	84.7 ±17.4	0.80
BMI (mean Kg/m²)	26.5 ±5.6	27.4.5	0.68
Affected knee (n)	R=5 knees, L= 5 knees	R=3 knees, L= 7 knees	

*Comparator group. R= right, L=left

All participants completed the trials with high compliance in wearing the insoles and the monitor. In addition, lateral wedged insole and neutral insole were found to be comfortable during walking by 75% and 90%, respectively, of individuals. There was no significant difference in the duration of daily insoles wear between lateral wedged insole group and neutral insole group ($p \geq 0.05$). (Table 4-3).

Table 4-3: Insoles users comfort and adherence of the participants to wearing insoles and monitor, the mean (±SD) of daily insoles/monitor use

	Neutral Insole (mean ±SD)	Lateral wedged insole (mean ±SD)	ActivPAL3 (mean)
Mean comfortable score (%)	90%	75%	====
Period 1 (hours/day)*	====	====	12-24
Period 2 (hours/day)**	7.26 (1.17)	6.52 (0.95)	12-24
Period 3 (hours/day) ♦	7.53 (1.90)	7.45 (1.80)	12-24

*Period 1: pre-baseline (pre-W0).
**Period 1: from week 0-1 (W0-W1).
♦Period 2: from week 0-6.

4.10.2. Comparison between wedged insole group and neutral insole group at baseline for primary outcome measures

At the baseline assessment, the mean differences of walking speed 0.032 m/s, EKAM 0.067 Nm/kg, KAAI 0.04 (Nm/kg).s, number of daily steps 517 steps/day and KOOS knee pain were 2.1 for lateral wedged insole group and neutral insole group. Therefore, there was no significant difference between groups at the baseline (when no intervention was applied) in term of primary outcomes ($p \geq 0.05$) of the study. (Table 4-4)

Table 4-4: Mean (SD) of outcomes at baseline for the groups and p-value (between both groups at baseline).

	Mean (SD)		
	wedged insole group	Neutral insole group	P-value*
speed (m/s)	0.87 (0.19)	0.83 (0.23)	0.73
External knee adduction moment Nm/kg	0.46 (0.11)	0.39 (0.12)	0.22
%BW.Ht	2.68 (0.71)	2.17 (0.90)	0.18
Knee adduction angular impulse (Nm/kg).s	0.28 (0.07)	0.25 (0.10)	0.39
No. of steps (steps/day)	6415 (2926)	6932 (3905)	0.74
Knee pain (KOOS)	51.9 (15.5)	49.8 (11.7)	0.742

*****Not significant value P≥0.05

4.10.3. Comparison of the groups at one week

The following will examine the differences between the two groups after wearing the interventions, for one week, to examine the short-term effect of the intervention.

4.10.3.1. Knee moment in frontal plane for the two groups

First peak in the EKAM

When assessing the EKAM between the two groups, the groups generally had no statistically significant effect on the first peak of the EKAM (p=0.730). The ANOVA analysis also showed that the main effect of duration of intervention (weeks) has a significant effect on the EKAM (p=0.004) and there was significant interaction between groups and weeks (p=0.002). The descriptive data is presented in table 4-5.

The data from the baseline assessment indicated that lateral wedged insole significantly reduced the first peak of the EKAM (mean difference 0.05 (0.04) Nm/kg, p=0.005) in comparison to the shod only by 12% (ranged 1.9%-27.7%). After wearing LWIs for one week, there was also a significant reduction (mean difference 0.05 (0.04) Nm/kg, p=0.001) in the first peak of the EKAM in comparison to the shod only at week one by 12% ranged 3.7%-24.9%). In addition, after wearing LWIs for one week, the first peak of the EKAM significantly reduced (mean difference 0.07 (0.05) Nm/kg, p=0.00) in comparison to the shod at baseline by 15% (ranged (-28.8%)-2.6%) (Figure 4-5a).

The data of the neutral group at baseline indicated that neutral insole did not change the first peak of the EKAM significantly (mean difference 0.001(0.01) Nm/kg, p= 0.76) in comparison to the shod only. After wearing neutral insoles for one week, there was no significant change (mean difference 0.003 (0.02) Nm/kg, p=0.67) in the first peak of the EKAM in comparison to the shod only at week one. In addition, after wearing neutral insoles for one week, the first peak of the EKAM did not change significantly (mean difference 0.001 (0.03) Nm/kg, p=0.94) in comparison to the shod at baseline (Figure 4-5b).

An independent t-test was conducted between the both groups for week one where the first peak of the EKAM was found to have significantly reduced in the LWI group compared to comparator group (p=0.004). After one week, the 1st peak of EKAM was decreased in eight individuals out of ten and four individuals out ten during walking in LWI group and comparator group, respectively, compared to the baseline. Whereas, from the data of baseline, the 1st peak of EKAM was decreased in all

individuals and four individuals out ten during walking in LWI group and comparator group, respectively, compared to shod only.

Second peak in the EKAM

The ANOVA analysis has showed that groups generally had no statistically significant effect on the second peak of the EKAM (p=0.28). The main effect of duration of intervention (weeks) has a significant effect on the second peak of the EKAM (p=0.01) with no interaction between groups and weeks (p=0.23). The descriptive data is presented in Table 4-5.

The data from the baseline assessment indicated that the lateral wedged insole reduced the second peak of the EKAM significantly (mean difference 0.05 (0.04) Nm/kg, p=0.003) in comparison to the shod only by 11% (ranged 0.0%-23.5%). After wearing LWIs for one week, there was a significant reduction (mean difference 0.06 (0.03) Nm/kg, p=0.001 in the second peak of the EKAM in comparison to the shod at week one by 11.7% (ranged (4.1%-26.5%). In addition, after wearing LWIs for one week, the second peak of the EKAM reduced significantly (mean difference 0.067 (0.06) Nm/kg, p=0.002) in comparison to the shod at baseline by 14.2% (ranged (-21.6%)-0.7%) (Figure 4-5a).

The data of the comparator group at baseline indicated that neutral insole did not change the second peak of the EKAM significantly (mean difference 0.004 (0.04) Nm/kg, p=0.76 in comparison to the shod only. After wearing neutral insoles for one week, there was no significant change (mean difference 0.001 (0.04) Nm/kg, p=0.89) in the second peak of the EKAM in comparison to the shod at week one. In addition, after wearing neutral insoles for one week, the second peak of the EKAM did not change significantly (mean difference 0.009 (0.09) Nm/kg, p=0.74) in comparison to shod (Figure 4-5b). There was no significant change in the second peak between groups (p=0.14).

Table 4-5: Mean (SD) EKAM (1st peak and 2nd peak) during walking for two groups after wearing insoles for one week.

EKAM	Mean (SD)							
	Baseline (week 0)				Week One			
	Wedged Group		Neutral Group		Wedged Group		Neutral Group	
	Shod	LWI	Shod	Neutral insole	Shod	LWI	Shod	Neutral insole
1st peak (Nm/kg)	0.46 (0.11)	0.40* (0.12)	0.39 (0.13)	0.39 (0.13)	0.44 (0.10)	0.39* (0.09)	0.38 (0.12)	0.39 (0.12)
2nd peak (Nm/kg)	0.49 (0.15)	0.43 (0.16)	0.37 (0.19)	0.36 (0.2)	0.47 (0.13)	0.42 (0.12)	0.36 (0.16)	0.36 (0.16)

***** Significant reduction compared to shod at baseline.

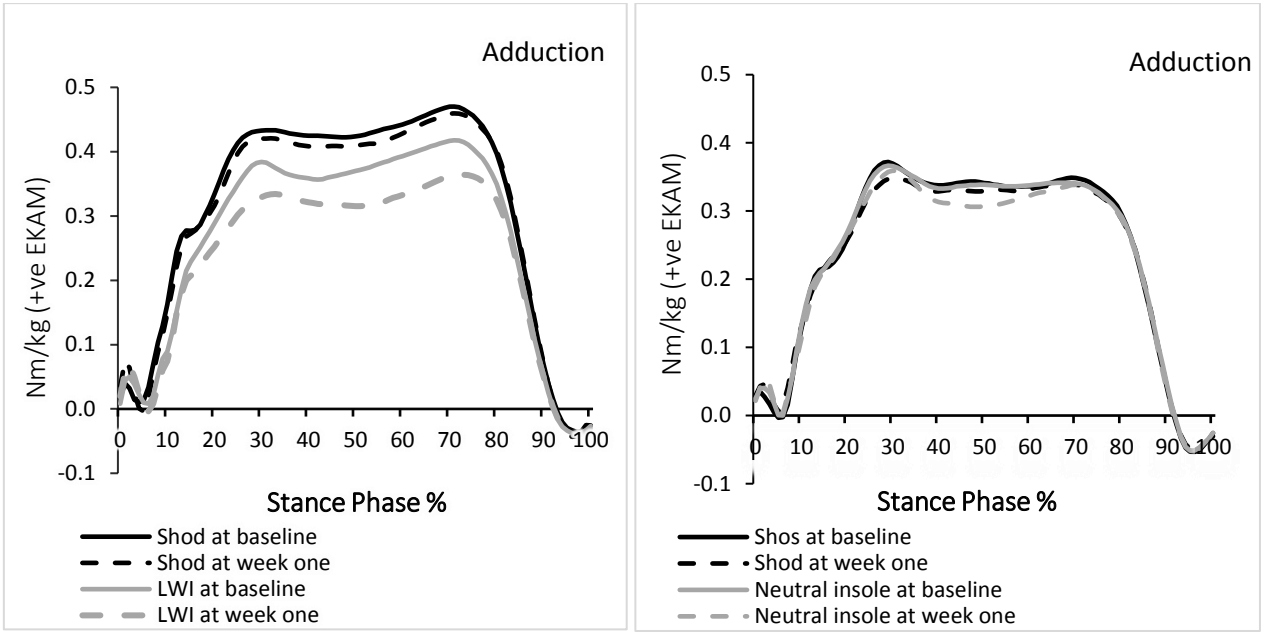


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Figure 4-5: The external knee adduction moment (EKAM) in frontal plane for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.3.2. Knee adduction angular impulse for the two groups

The loading for the whole of the duration of the stance phase was assessed with the knee adduction angular impulse.

The ANOVA analysis has showed that the groups generally had no statistically significant effect on the KAAI (p=0.84) whereas the main effect of duration of intervention (weeks) has a significant effect on the KAAI (p=0.004). In addition, groups and weeks interaction had an effect on the KAAI (p=0.051) but not statically significant. The descriptive data is presented in Table 4-6.

The data from baseline indicated that the lateral wedged insole reduced the KAAI significantly (mean difference 0.03 (0.04) Nm/kg*s, p=0.026) in comparison to the shod only by 11.6% (ranged (-30%)-0.0). After wearing LWIs for one week, there was a significant reduction (mean difference 0.05 (0.05) Nm/kg*s, p=0.01) in the KAAI in comparison to the shod only at week one by 16.8% (ranged (-35.3%)-0.0%). In addition, after wearing LWIs for one week, the KAAI reduced significantly (mean difference 0.05 (0.04) Nm/kg*s, p=0.001) in comparison to the shod at baseline by 17.8% (ranged (-31%)-25.6%).

The comparator group at baseline indicated that the neutral insole did not change the KAAI significantly (mean difference 0.01 (0.01) Nm/kg*s, p= 0.11) in comparison to the shod only. After

wearing neutral insoles for one week, there was no significant change (mean difference 0.02 (0.03) Nm/kg*s, p=0.09) in the KAAI in comparison to the shod only at week one. In addition, after wearing neutral insoles for one week, the KAAI did not change significantly (mean difference 0.017 (0.03) Nm/kg*s, p=0.21) in comparison to the shod at baseline.

There was no significant difference between LWI group and comparator group after one week (p=0.09).

Table 4-6: Mean (SD) KAAI during walking for two groups after wearing insoles for one week.

KAAI	Mean (SD)							
	Baseline				Week One			
	Wedged Group		Neutral Group		Wedged Group		Neutral Group	
	Shod	LWI	Shod	Neutral insole	Shod	LWI	Shod	Neutral insole
KAAI (Nm/kg)*s	0.28 (0.07)	0.25* (0.08)	0.25 (0.1)	0.24 (0.1)	0.28 (0.08)	0.23* (0.07)	0.25 (0.09)	0.23 (0.09)

***** Significant reduction compared to shod at baseline

4.10.3.3. Knee moment in sagittal plane for the two groups

With the recent papers highlighting that any change in EKAM, one should also be aware of change in the sagittal plane knee moment, this was assessed between groups and time points.

The groups generally had no statistically significant effect on the maximum knee flexion moment (p=0.86) or on the maximum knee extension moment (p=0.82). Whereas the main effect of duration of intervention (time) has a significant effect on the maximum knee flexion moment (p=0.02). The ANOVA analysis has also showed that there was no significant interaction between groups and weeks in the maximum knee flexion moment (p=0.55) or in the maximum knee extension moment (p=0.24) (figure 4-6). The descriptive data is presented in table 4-7.

After one week, there was no significant difference within group or between groups in maximum knee flexion moment or maximum knee extension moment with either insole.

Table 4-7: Mean (SD) knee moment in sagittal plane during walking for the two groups after wearing insoles for one week.

	Mean (SD)							
	Baseline				Week One			
	Wedged Group		Neutral Group		Wedged Group		Neutral Group	
	Shod	LWI	Shod	Neutral insole	Shod	LWI	Shod	Neutral insole
Knee flexion moment (Nm/kg)	0.46 (0.27)	0.49 (0.28)	0.50 (0.23)	0.54 (0.27)	0.49 (0.26)	0.53 (0.27)	0.49 (0.24)	0.52 (0.24)
Knee extension moment (Nm/kg)	-0.34 (0.18)	-0.30 (0.15)	-0.32 (0.14)	-0.34 (0.14)	-0.32 (0.15)	-0.30 (0.17)	-0.31 (0.20)	-0.35 (0.14)

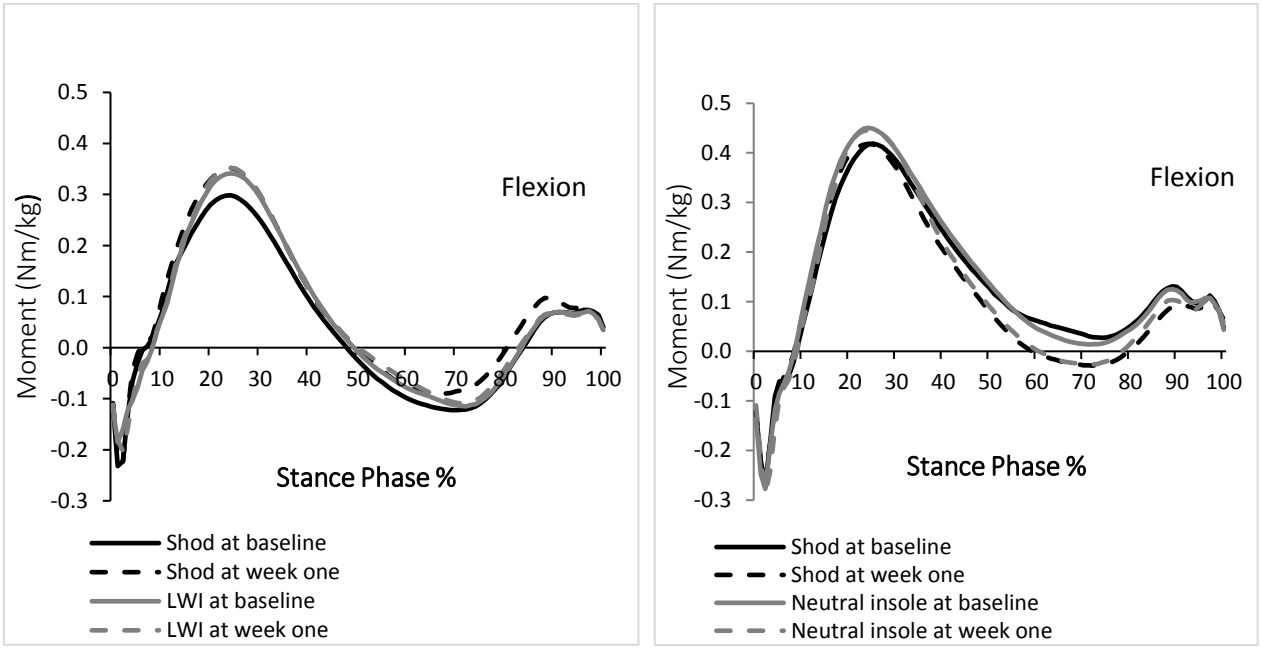

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Figure 4-6: The knee moment in sagittal plane for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.3.4. Vertical ground reaction force for the two groups

One of the mechanisms that would alter the EKAM and could be a contra-indicator in the results is the vertical ground reaction force. This force, if changed significantly, between groups, may be a reason for a change the thus needs to be assessed. Descriptive data of GRF results for both groups are illustrated in table 4-8.

There was no significant difference between groups ($p \geq 0.05$) in early stance, mid-stance-late stance phase of the GRF. The ANOVA analysis has also showed that there was no significant interaction between groups and weeks and the main effect of weeks was not significant on the early stance, mid-stance-late stance phase of the GRF ($p \geq 0.05$) (Figure 4-7).

After wearing insoles (either LWI or neutral insole) for one week, there were no significant change in early stance, mid-stance-late stance phase of the GRF compared to baseline and between groups.

Table 4-8: Mean (SD) vertical ground reaction force for two group after wearing insoles for one week

GRF	Mean (SD)							
	Baseline				Week One			
	Wedged Group		Neutral Insole Group		Wedged Group		Neutral Insole Group	
	Shod	LWI	Shod	Neutral insole	Shod	LWI	Shod	Neutral insole
Early stance (*BW)	1.02 (0.06)	1.05 (0.07)	1.04 (0.05)	1.03 (0.09)	1.02 (0.08)	1.05 (0.09)	1.06 (0.06)	1.05 (0.1)
Mid-stance (*BW)	0.87 (0.08)	0.85 (0.08)	0.89 (0.07)	0.85 (0.08)	0.86 (0.09)	0.84 (0.09)	0.88 (0.09)	0.87 (0.1)
Late stance (*BW)	1.04 (0.05)	1.04 (0.04)	1.05 (0.06)	1.04 (0.1)	1.04 (0.05)	1.05 (0.04)	1.06 (0.07)	1.04 (0.1)

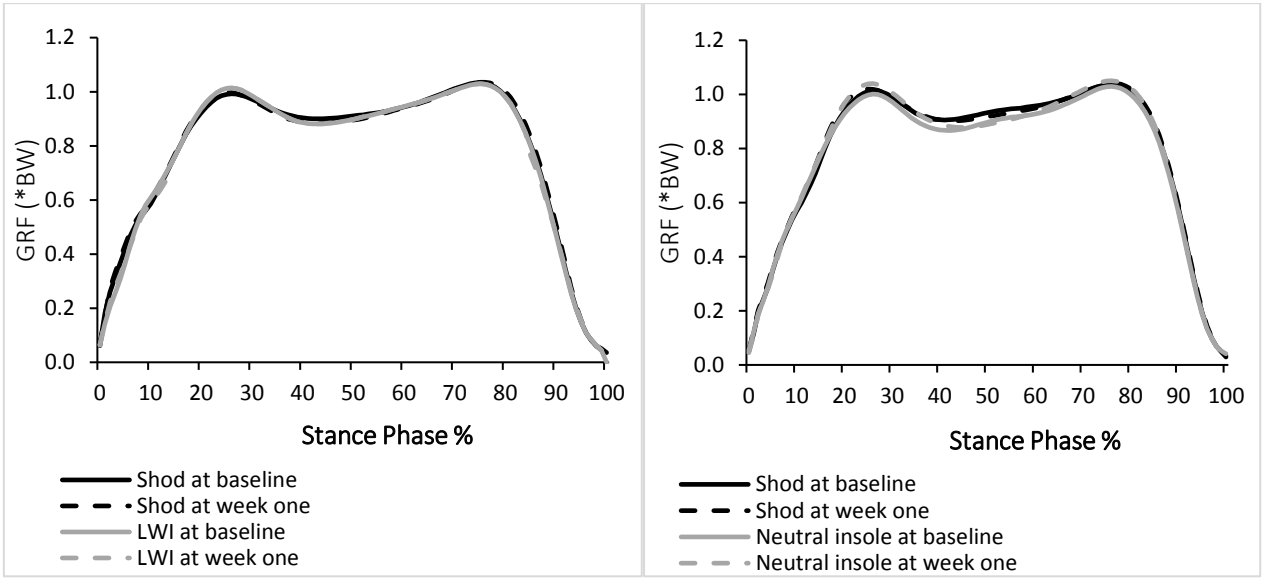

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Figure 4-7: The vertical ground reaction force for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.4. Comparison of the groups at six weeks

The following will examine the differences between the two groups after wearing the intervention to examine the six weeks effect of the interventions.

4.10.4.1. Knee moment in frontal plane for the two groups

First peak in the EKAM

The ANOVA analysis has showed that the groups generally had no statistically significant effect on the first peak of the EKAM (p=0.730) whereas the main effect of duration of intervention (weeks) has a significant effect on the EKAM (p=0.004) and there was significant interaction between groups and weeks (p=0.002). The descriptive data is presented in Table 4-9.

After wearing LWIs for six weeks, there was significant reduction (mean difference 0.06 (0.05) Nm/kg, p=0.003 in the first peak of the EKAM in comparison to the shod only at week six by 14.6% (ranged (-28.7%)-2.3%). In addition, after wearing LWIs for six weeks, the first peak of the EKAM significantly reduced (mean difference 0.08 (0.076) Nm/kg, p=0.004) in comparison to the shod at baseline by16.8% (ranged (-34%)-13.6%) (Figure 4-8a).

After wearing neutral insoles for six weeks, there was no significant change (mean difference 0.001 (0.01) Nm/kg, p=0.92 in the first peak of the EKAM in comparison to the shod only at week six. In addition, after wearing neutral insoles for six weeks, the first peak of the EKAM did not change significantly (mean difference 0.003 (0.02) Nm/kg, p=0.78) in comparison to the shod at baseline (Figure 4-8b).

After wearing LWIs for six weeks, the first peak of the EKAM reduced significantly in LWI group compared to comparator group (p=0.008). After six weeks, the 1st peak of EKAM was decreased in eight individuals out of ten and two individuals out ten during walking in LWI group and comparator group, respectively, compared to the baseline.

Second peak in the EKAM

The ANOVA analysis has showed that groups generally had no statistically significant effect on the second peak of the EKAM (p=0.28). The main effect of duration of intervention (weeks) has a significant effect on the second peak of the EKAM (p=0.01) with no interaction between groups and weeks (p=0.23). The descriptive data is presented in table 4-9.

After wearing LWIs for six weeks, there was a significant reduction (mean difference 0.06 (0.05) Nm/kg, p=0.002) in the second peak of the EKAM in comparison to the shod only at week six by 12.2% (ranged (-22%)-1.6%). In addition, after wearing LWIs for six weeks, the second peak of the EKAM significantly reduced (mean difference 0.05 (0.06) Nm/kg, p=0.04) in comparison to the shod at baseline by 9.9% (ranged (-25.5%)-3.7%) (Figure 4-8a).

After wearing neutral insoles for six weeks, there was no significant change (mean difference Nm/kg0.01 (0.04), p=0.60) in the second peak of the EKAM in comparison to the shod only at week six. In addition, after wearing neutral insoles for six weeks, the second peak of the EKAM did not significantly change (mean difference 0.005 (0.06) Nm/kg, p=0.82) in comparison to the shod at baseline (Figure 4-8b).

There was no significant difference between groups in the second peak of the EKAM after six weeks.

Table 4-9: Mean (SD) EKAM (1st peak and 2nd peak) during walking for two groups after wearing insoles for six weeks.

EKAM	Mean (SD)					
	Baseline (week 0)		Week Six			
	Wedged Group	Neutral Group	Wedged Group		Neutral Group	
			Shod	LWI	Shod	Neutral insole
1st peak (Nm/kg)	0.46 (0.11)	0.39 (0.13)	0.44 (0.13)	0.38* (0.11)	0.39 (0.12)	0.39 (0.13)
2nd peak (Nm/kg)	0.49 (0.15)	0.37 (0.19)	0.50 (0.17)	0.44* (0.16)	0.37 (0.19)	0.37 (0.16)

***** Significant reduction compared to baseline

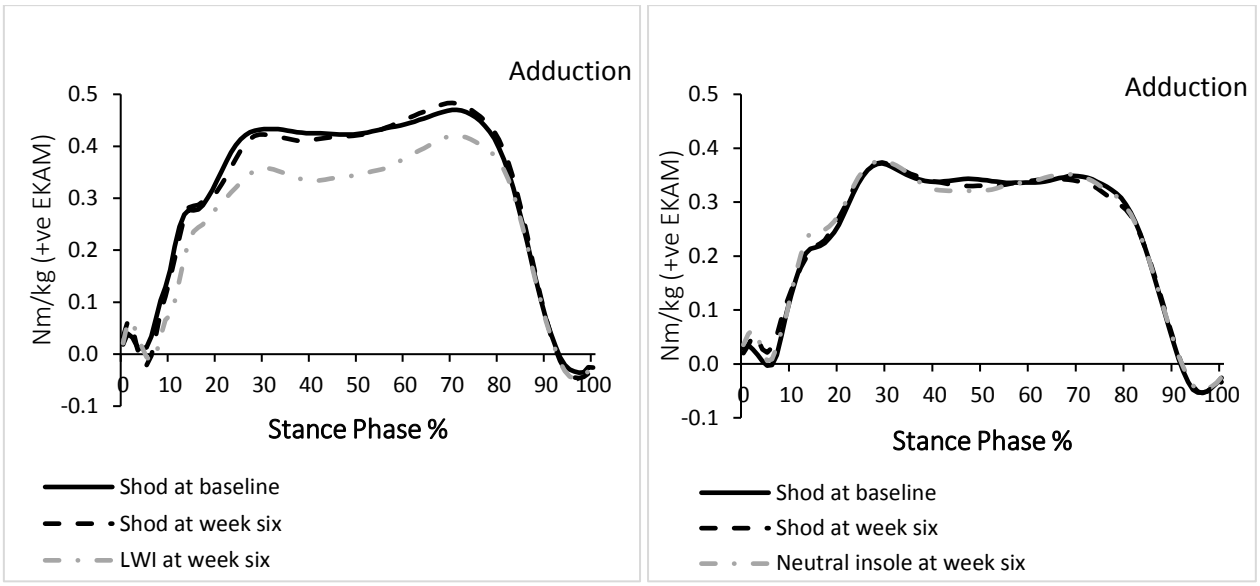

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Figure 4-8: The external knee adduction moment (EKAM) in frontal plane for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.4.2. Knee adduction angular impulse for the two groups

The ANOVA analysis has showed that groups generally had no statistically significant effect on the KAAI (p=0.84) whereas the main effect of duration of intervention (weeks) has a significant effect on the KAAI (p=0.004). There was interaction between groups and weeks (p=0.051) but not statically significant. The descriptive data is presented in table 4-10.

After wearing LWIs for six weeks, there was a significant reduction (mean difference 0.04 (0.03) Nm/kg*s, p=0.005) in the KAAI in comparison to the shod only at week six by 14.3% (ranged 0.0%-33.3%). In addition, after wearing LWIs for six weeks, the KAAI significantly reduced (mean difference 0.062 (0.04) Nm/kg*s, p=0.000) in comparison to the shod at baseline by 22% (ranged 3.4%-43.8%). Importantly, the KAAI reduced significantly after wearing LWIs for six weeks compared to baseline and comparator groups (p=0.01).

After wearing neutral insoles for six weeks, there was no significant change (mean difference 0.01 (0.04) Nm/kg*s, p=0.32) in the KAAI in comparison to the shod only at week six. In addition, after wearing neutral insoles for six weeks, the KAAI did not change significantly (mean difference 0.009 (0.03) Nm/kg*s, p=0.45) in comparison to the shod at baseline.

Table 4-10: Mean (SD) KAAI during walking for two groups after wearing insoles for six weeks.

KAAI	Mean (SD)					
	Baseline		Week Six			
	Wedged Group	Neutral Group	Wedged Group		Neutral Group	
			Shod	LWI	Shod	Neutral insole
KAAI Nm/kg*s	0.28 (0.07)	0.25 (0.1)	0.26 (0.08)	0.22* (0.08)	0.25 (0.12)	0.24 (0.09)

***** Significant reduction compared to baseline

4.10.4.3. Knee moment in sagittal plane for the two groups

The groups generally had no statistically significant effect on the maximum knee flexion moment ($p=0.86$) or on the maximum knee extension moment ($p=0.82$). Whereas the main effect of duration of intervention (time) has a significant effect on the maximum knee flexion moment ($p=0.02$) only compared to baseline. The ANOVA analysis has also showed that there was no significant interaction between groups and weeks in the maximum knee flexion moment ($p=0.55$) or in the maximum knee extension moment ($p=0.24$). The descriptive data is presented in Table 4-11.

After wearing LWI for six weeks, the maximum knee flexion moment did not significantly increase (mean difference 0.039 (0.01) Nm/kg, $p= 0.14$) in comparison to the shod only at week six with the maximum knee flexion moment slightly increasing (average increased was 7.2 %, ranged (-14%)-26%). In addition, after wearing LWI for six weeks, the maximum knee flexion moment significantly increased (mean difference 0.11 (0.12) Nm/kg, $p=0.01$) in comparison to the shod at baseline by 22.6% (ranged (-13.9%)-40%) with no significant change was seen in comparator group compared to time points ($p\geq 0.05$) (Figure 4-9). After six weeks, there was no significant differences between groups in maximum knee flexion moment or maximum knee extension moment.

Table 4-11: Mean (SD) knee moment in sagittal plane during walking for two groups after wearing insoles for six weeks.

	Mean (SD)					
	Baseline		Week Six			
			Wedged Group		Neutral Group	
	Wedged Group	Neutral Group	Shod	LWI	Shod	Neutral insole
Knee flexion moment (Nm/kg)	0.46 (0.27)	0.50 (0.23)	0.53 (0.27)	0.57* (0.28)	0.54 (0.26)	0.57 (0.26)
Knee extension moment (Nm/kg)	-0.34 (0.18)	-0.32 (0.14)	-0.34 (0.19)	-0.35 (0.18)	-0.28 (0.21)	-0.34 (0.16)

***** Significant difference compared to baseline.

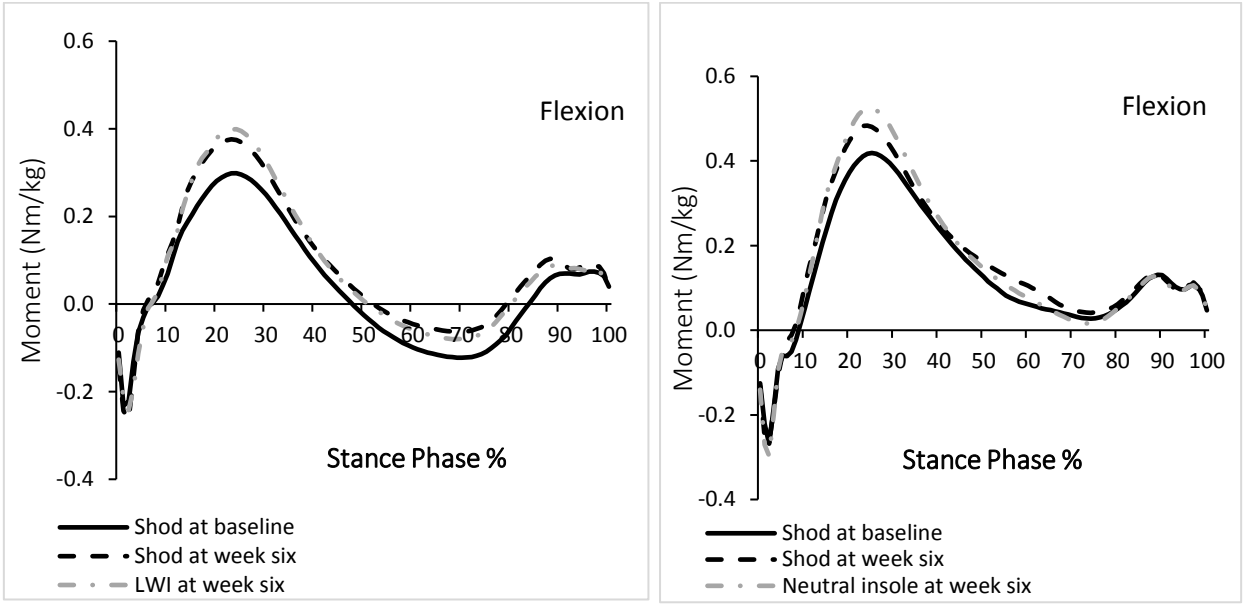

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Figure 4-9: The knee moment in sagittal plane for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.4.4. Vertical ground reaction force for the two groups

There was no significant difference between groups ($p \geq 0.05$) in early stance, mid-stance-late stance phase of the GRF. The ANOVA analysis has also showed that there was no significant interaction between groups and weeks and the main effect of weeks was not significant on the early stance, mid-stance-late stance phase of the GRF ($p \geq 0.05$). The descriptive data is presented in table 4-12.

After wearing insoles (either LWI or neutral insole) for six weeks, there were no significant changes in early stance, mid-stance-late stance phase of the GRF compared to baseline and comparator group (Figure 4-10).

Table 4-12: Mean (SD) vertical ground reaction force for two groups after wearing insoles for six weeks.

GRF	Mean (SD)					
	Baseline		Week Six			
	Wedged Group	Neutral Group	Wedged Group		Neutral Group	
			Shod	LWI	Shod	Neutral insole
Early Stance (*BW)	1.02 (0.06)	1.04 (0.05)	1.05 (0.1)	1.06 (0.09)	1.06 (0.09)	1.05 (0.12)
Mid-stance (*BW)	0.87 (0.08)	0.89 (0.07)	0.84 (0.06)	0.83 (0.07)	0.87 (0.1)	0.86 (0.11)
Late Stance (*BW)	1.04 (0.05)	1.05 (0.06)	1.05 (0.08)	1.06 (0.06)	1.05 (0.8)	1.04 (0.12)

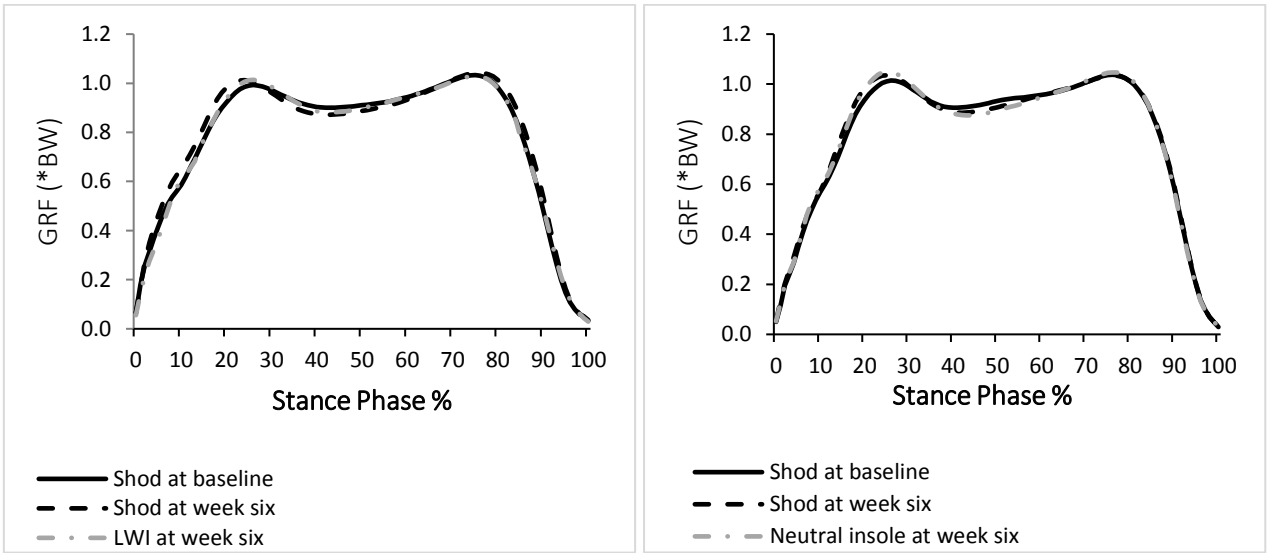

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Figure 4-10: The vertical ground reaction force for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.5. Volume of level of physical activity

4.10.5.1. Number of steps

The mean, SD, mean difference, p-values and changes in the average number of steps (per day) for both groups are shown in table 4-13 and table 4-14. Table 4-15 and figures 4-11 & 4-12 show the mean number of steps for all participants at baseline, week one, and week six for both groups (LWI group and comparator group).

The groups (LWI and comparator groups) had no statistically significant effect on the average number of steps per day (p=0.610). The main effect of duration of intervention "weeks" (baseline, week one, and week six) has no significant effect on the number of steps (p=0.330) but there was a significant interaction between the groups and weeks (p=0.003).

After wearing LWIs for one week, the average number of steps per day did not change significantly (mean difference 603 steps/day, p=0.236) in comparison to baseline, the number of steps increased slightly (average increase was 9.4%, range -4%-92%). After wearing LWIs for six weeks, the number of steps significantly increased (mean difference 1,525 steps/day, p=0.000) in comparison to baseline by 23.8% (range -18%-96%).

After wearing neutral insole for one week, the average number of steps (per day) did not change significantly (mean difference -805 steps/day, p=0.119) in comparison to baseline, although the number of steps decreased slightly (average decrease was 11.6%, range -33%-17%). After wearing neutral insole for six week, the number of steps significantly decreased (mean difference -810 steps/day, p=0.032) in comparison to baseline by 11.7% (range -54%-2%).

There was no significant differences in the changes between week one and baseline between LWI group and comparator group (mean difference 1,408 steps/day, p=0.058). However, the changes between week six and baseline in the average number of steps per day significantly increased in LWI group compared to comparator group (mean difference 2,335 steps/day, p=0.000).

Table 4-13: Mean (SD), mean difference and p-value of the number of steps for groups

	Mean (SD)						Mean difference within groups			
	Week 0		Week 1		Week 6		week 0 vs. week 1		week 0 vs. week-6	
	LWI	Neutral	LWI	Neutral	LWI	Neutral	LWI	neutral	LWI	Neutral
No. of steps (steps/day)	6,415 (2,926)	6,932 (3,905)	7,018 (2,582)	6,126 (2,730)	7,940 (2,904)	6,121 (4,161)	603 0.236	-805 0.119	1,525 **0.000***	-810 **0.032***

*Significant difference value.

Table 4-14: The mean of the number of steps (steps/day) for individuals

Subject	LWI Group			Neutral Insole Group		
	Baseline	Week 1	Week 6	Baseline	Week 1	Week 6
1	2,575	4,456	5,041	6,667	5,677	5,542
2	11,723	11,270	13,548	5,646	6,556	5,534
3	4,851	5,146	6,590	7,220	5,841	6,195
4	6,054	4,194	4,979	15,659	10,507	15,439
5	6,767	7,544	9,297	3,830	3,801	1,768
6	5,903	6,737	8,829	3,012	3,190	2,989
7	3,579	6,882	5,580	10,815	10,413	10,986
8	10,849	11,008	10,736	8,349	7,872	6,153
9	4,707	4,600	5,299	3,459	4,032	3,221
10	7,143	8,340	9,503	4,661	3,375	3,388
Mean (SD)	6,415 (2,926)	7,018 (2,582)	7,940 (2,904)	6,932 (3,905)	6,126 (2,730)	6,121 (4,161)

Table4-15: The differences in the number of steps for all participants for both groups.

Subject	Difference in number of steps (steps/day)			
	LWI Group		Neutral Insole Group	
	W1-Baseline	W6-Baseline	W1-Baseline	W6-Baseline
1	1,881	2,466	-991	-1,126
2	-453	1,826	911	-112
3	295	1,739	-1,379	-1,025
4	-1,859	-1,075	-5,152	-219
5	777	2,530	-28	-2,062
6	834	2,926	179	-23
7	3,304	2,001	-402	172
8	159	-113	-477	-2,196
9	-107	592	573	-239
10	1,197	2,360	-1,286	-1,273
Mean	603	1,525	-805	-810

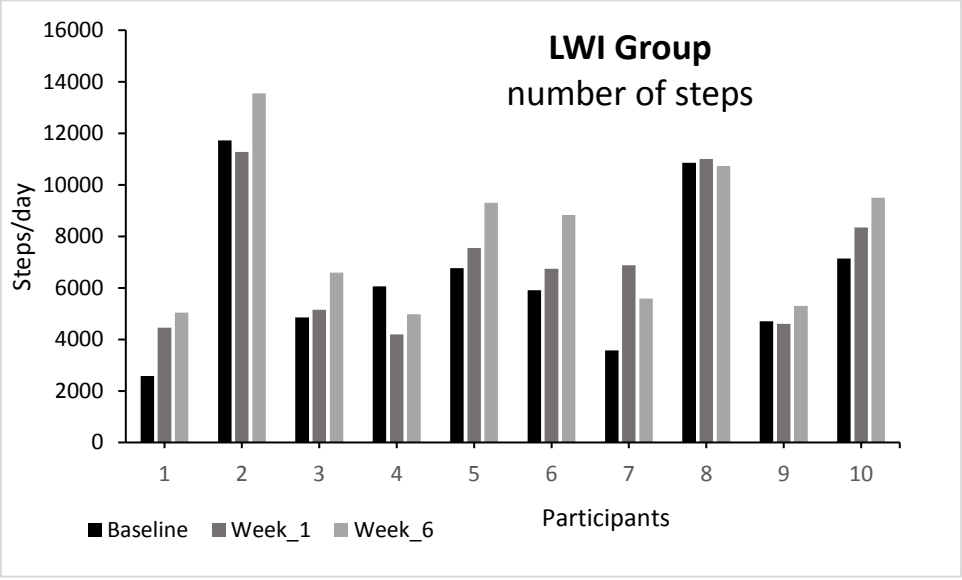

Figure 4-11: The mean of number of steps for all participants for baseline, week 1, and week 6 in LWI group.

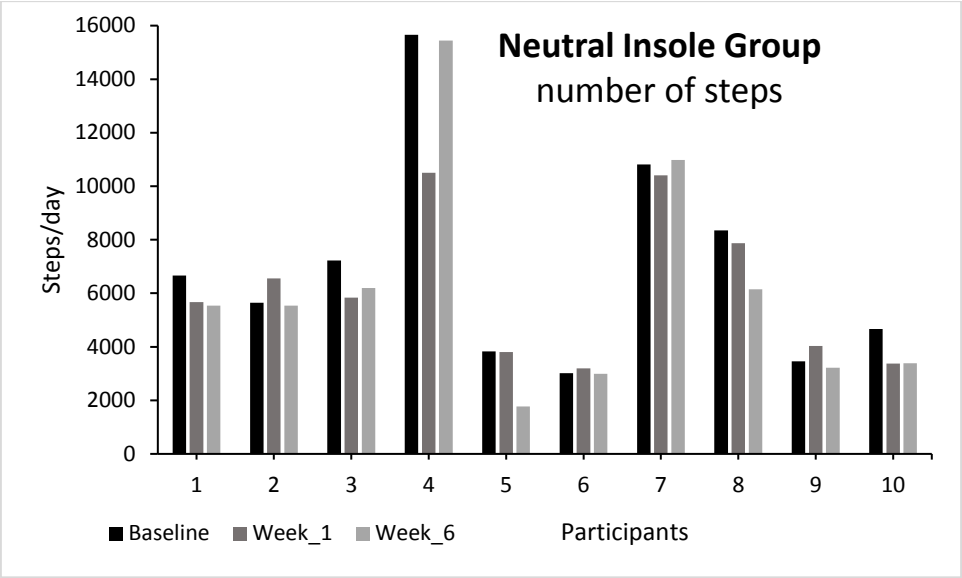

Figure 4-12: The mean of number of steps for all participants for baseline, week 1, and week 6 in comparator group.

4.10.5.2. Sedentary time

The mean, SD, mean difference, and changes in the sedentary time per day for both groups are shown in table 4-16 and table 4-17. Table 4-18 and figures 4-13 & 4-14 show the average of sedentary time for all participants at baseline, week one, and week six for both groups (LWI group and comparator group).

The groups (LWI and comparator group) had no statistically significant effect on the average sedentary time (p=0.851). The main effect of duration of intervention "weeks" (baseline, week one, and week six) had no significant effect on the sedentary time (p=0.480) and there was no significant interaction between the groups and weeks (p=0.178).

After wearing LWIs for one week, the average of sedentary time did not change significantly (mean difference 9 min/day, p=0.438) in comparison to baseline, although the sedentary time deceased slightly (average decrease was 0.8%, range -5%-7%). After wearing LWIs for six weeks, sedentary time did not change significantly (mean difference 35 min/day, p=0.184) in comparison to baseline, although the sedentary time deceased slightly (average decrease was 3.1 %, range -11%-12%).

After wearing neutral insole for one week, the average sedentary time did not change significantly (mean difference 18 min/day, p=0.136) in comparison to baseline, the sedentary time decreased slightly (average decrease was 1.5%, range -4%-3%). After wearing neutral insole for six weeks,

sedentary time did not change significantly (mean difference 7 min/day, p=0.788) in comparison to baseline, although the sedentary time increased slightly (average increase was 0.6%, range -9%-15%)

There were no significant differences in the changes between baseline compared to week one or week six between LWI group and comparator group.

Table 4-16: Mean (SD) and mean differences of the sedentary for groups

	Mean (SD)						Mean difference within groups			
	Week 0		Week 1		Week 6		week 0 vs. Week 1		week 0 vs. Week 6	
	LWI	Neutral	LWI	Neutral	LWI	Neutral	LWI	Neutral	LWI	Neutral
Sedentary time (min/day)	1,156 (104)	1,152 (59)	1,147 (89)	1,134 (59)	1,121 (103)	1,159 (114)	-9 0.438	-18 0.136	-35 0.184	7 0.788

Table 4-17: The mean of the sedentary time (min/day) for individuals

Subject	LWI Group			Neutral Insole Group		
	Baseline	Week 1	Week 6	Baseline	Week 1	Week 6
1	1,205	1,142	1,175	1,210	1,208	1,247
2	1,069	1,026	956	1,182	1,163	1,238
3	1,137	1,099	1,014	1,089	1,079	988
4	1,271	1,261	1,188	1,097	1,079	1,085
5	1,095	1,140	1,108	1,167	1,157	1,339
6	1,065	1,140	1,195	1,095	1,125	1,095
7	1,315	1,269	1,278	1,183	1,137	1,074
8	1,096	1,075	1,061	1,070	1,023	1,066
9	1,282	1,261	1,203	1,240	1,198	1,176
10	1,026	1,058	1,029	1,186	1,173	1,281
Mean (SD)	1,156 (104)	1,147 (89)	1,121 (103)	1,152 (59)	1,134 (59)	1,159 (114)

Table4-18: The differences in the sedentary time for all participants for both groups.

Subject	Difference in sedentary time (min/day)			
	LWI Group		Neutral Insole Group	
	W1-Baseline	W6-Baseline	W1-Baseline	W6-Baseline
1	-63	-30	-2	37
2	-43	-113	-20	56
3	-39	-123	-10	-101
4	-10	-83	-18	-12
5	46	14	-10	172
6	75	130	31	1
7	-46	-37	-46	-109
8	-21	-35	-46	-4
9	-21	-80	-42	-64
10	32	3	-13	95
Mean	-9	-35	-18	7

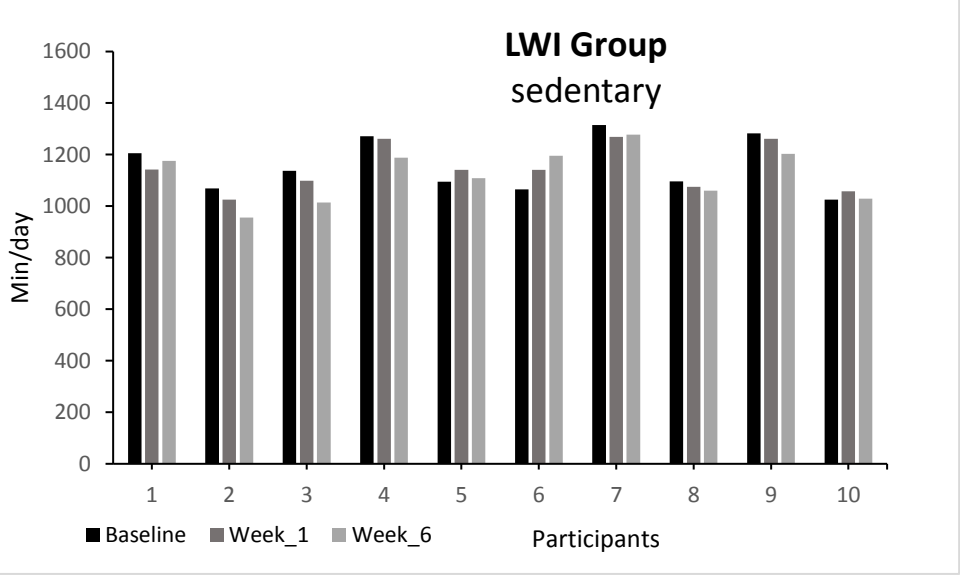

Figure 4-13: The mean of sedentary time for all participants for baseline, week 1, and week 6 in LWI group.

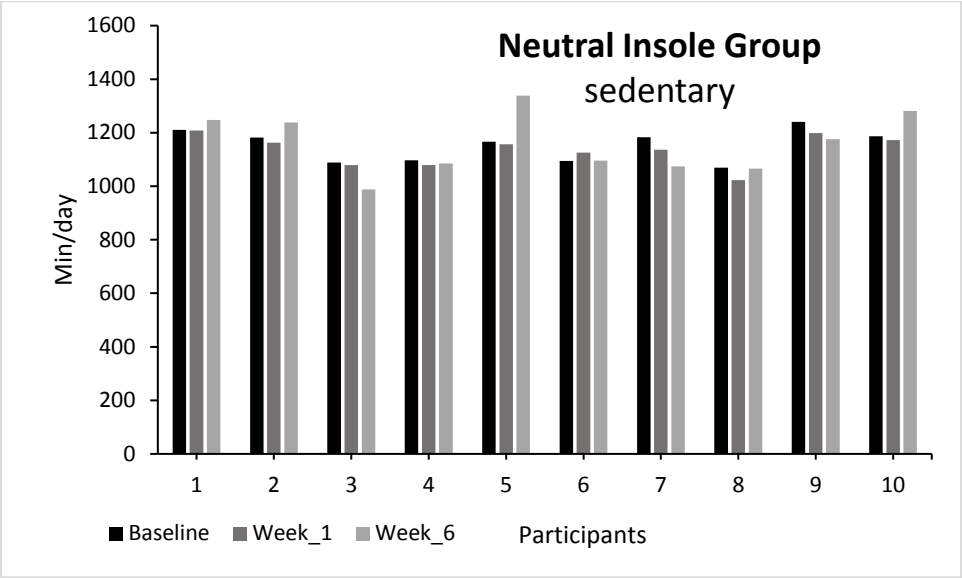

Figure 4-14: The mean of sedentary time for all participants for baseline, week 1, and week 6 in comparator group.

4.10.5.3. Up-right time

The mean, SD, mean difference, and changes in the upright time per day for both groups are shown in table 4-19 and table 4-20. Table 4-21 and figures 4-15 & 4-16 show the average of upright time for all participants at baseline, week one, and week six for both groups (LWI group and comparator group).

The groups (LWI and comparator groups) had no statistically significant effect on the average upright time (p=0.692). The main effect of duration of intervention "weeks" (baseline, week one, and week six) had no significant effect on the upright time (p=0.405) and there was a no significant interaction between the groups and weeks (p=0.377).

After wearing LWIs for one week, the average upright time did not change significantly (mean difference 9 min/day, p=0.536) in comparison to baseline, although the upright time increased slightly (average increase was 3.2%, range -8%-37%). After wearing LWIs for six week, upright time did not change significantly (mean difference 35 min/day, p=0.202) in comparison to baseline, although the upright time increased slightly (average increase was 12.5%, range -35%-50%).

After wearing neutral insole for one week, the average upright time did not change significantly (mean difference 14 min/day, p=0.342) in comparison to baseline, although the upright time increased slightly (average increase was 5.0%, range -4%-29%). After wearing neutral insole for six

weeks, the upright time did not change significantly (mean difference 3 min/day, p=0.912) in comparison to baseline, although the upright time increased slightly (average increase was 1.1%, range -63%- 43%).

There were no significant differences in the changes between baseline compared to week one or week six between LWI group and comparator group.

Table 4-19: Mean (SD), and mean differences of the upright for groups

	Mean (SD)						Mean difference within groups			
	Week 0		Week 1		Week 6		week 0 vs. Week 1		week 0 vs. Week 6	
	LWI	Neutral	LWI	Neutral	LWI	Neutral	LWI	Neutral	LWI	Neutral
Upright time (min/day)	284 (104)	278 (57)	293 (89)	292 (71)	319 (103)	281 (114)	9 0.536	14 0.342	35 0.202	3 0.912

Table 4-20: The mean of the upright time (min/day) for individuals

Subject	LWI Group			Neutral Insole Group		
	Baseline	Week 1	Week 6	Baseline	Week 1	Week 6
1	235	298	265	230	232	193
2	371	414	484	258	277	202
3	303	341	426	351	361	452
4	169	179	252	343	328	355
5	345	300	332	273	283	101
6	375	300	245	245	315	345
7	125	171	162	257	303	366
8	344	365	379	370	417	374
9	158	179	237	200	242	264
10	414	382	411	254	162	159
Mean (SD)	284 (104)	293 (89)	319 (103)	278 (57)	292 (71)	281 (114)

Table 4-21: The differences in the upright time for all participants for both groups.

Subject	Differences in up-right time (min/day)			
	LWI Group		Neutral Insole Group	
	W1-Baseline	W6-Baseline	W1-Baseline	W6-Baseline
1	63	30	2	-37
2	43	113	20	-56
3	39	123	10	101
4	10	83	-15	12
5	-45	-14	10	-172
6	-75	-130	70	100
7	46	37	46	109
8	21	35	46	4
9	21	80	42	64
10	-32	-3	-92	-95
Mean	9	35	14	3

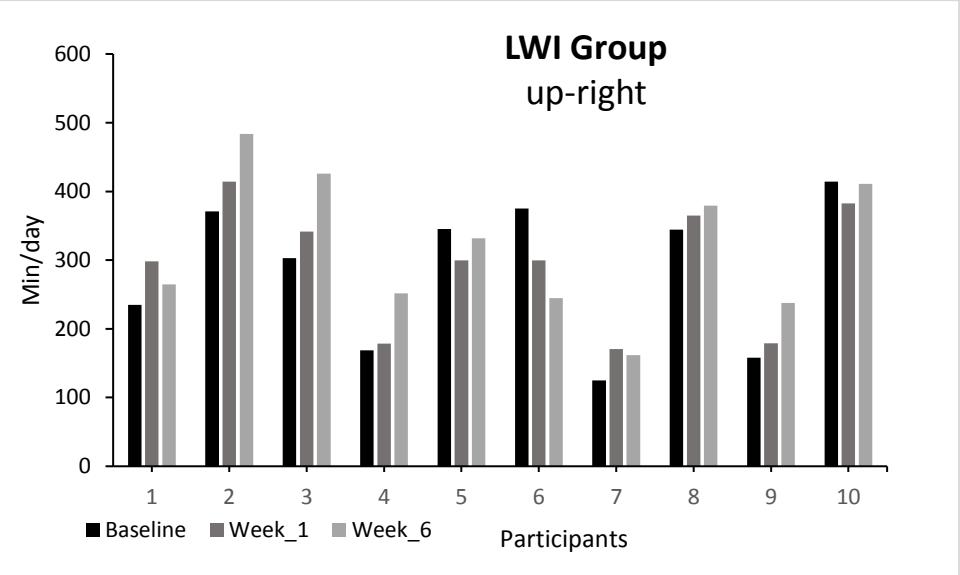

Figure 4-15: The mean of up-right time for all participants for baseline, week 1, and week 6 in LWI group.

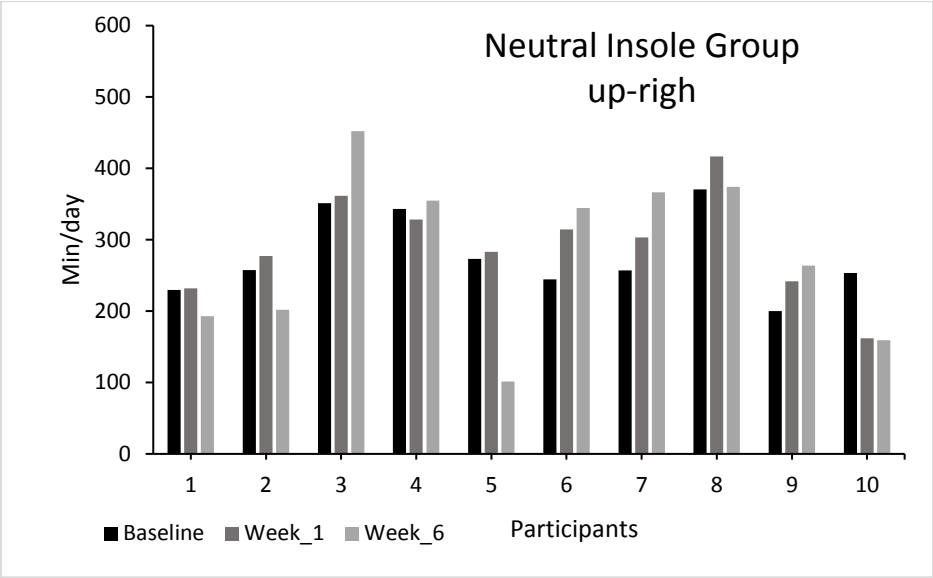

Figure 4-16: The mean of upright time for all participants for baseline, week 1, and week 6 in comparator group.

4.10.5.4. Stepping time

The mean, SD, mean difference, p-value and changes in the stepping time per day for both groups are shown in table 4-22 and table 4-23. Table 4-24 and figures 4-17 & 4-18 show the average of stepping time for all participants at baseline, week one, and week six for both groups (LWI group and comparator group).

The groups (LWI and comparator groups) had no statistically significant effect on the average stepping time (p=0.787). The main effect of duration of intervention "weeks" (baseline, week one, and week six) had no significant effect on the stepping time (p=0.339), however, there was a significant interaction between the groups and weeks (p=0.003).

After wearing LWIs for one week, the average stepping time did not change significantly (mean difference 8 min/day, p=0.092) in comparison to baseline, although the stepping time increased slightly (average increase was 9.8%, range -24%- 73%). After wearing LWIs for six weeks, the stepping time increased significantly (mean difference 17 min/day, p=0.001) in comparison to baseline by 20.7% (range -10%-62%).

After wearing neutral insole for one week, the average stepping time did not change significantly (mean difference 6 min/day, p=0.174) in comparison to baseline, although the stepping time decreased slightly (average decrease was 6.8%, range -26%-16%). After wearing neutral insole for

six weeks, the stepping time did not change significantly (mean difference 8 min/day, p=0.094) in comparison to baseline, although the stepping time decreased slightly (average decrease was 8.4%, range -48%-15%).

There was a significant increase in the changes between week one and baseline between LWI group and comparator group (mean difference 14 min/day, p=0.036). In addition, the changes between week six and baseline in the average stepping time increased significantly in LWI group compared to comparator group (mean difference 25 min/day, p=0.001).

Table 4-22: Mean SD), mean differences and p-value of the stepping time for groups

	Mean (SD)						Mean difference within groups			
	Week 0		Week 1		Week 6		week 0 vs. Week 1		week 0 vs. Week 6	
	LWI	Neutral	LWI	Neutral	LWI	Neutral	LWI	Neutral	LWI	Neutral
stepping time (min/day)	81 (30)	90 (41)	89 (28)	84 (34)	98 (33)	82 (45)	8 0.092	-6 0.174	17 **0.001***	-8 0.094

*Significant difference value

Table 4-23: The mean of the stepping time (min/day) for individuals

Subject	LWI Group			Neutral Insole Group		
	Baseline	Week 1	Week 6	Baseline	Week 1	Week 6
1	39	61	63	96	87	82
2	133	133	164	76	87	73
3	77	81	102	89	76	80
4	66	50	60	160	126	166
5	90	96	112	50	50	26
6	76	82	98	44	48	46
7	50	87	72	127	128	146
8	118	120	118	141	131	108
9	60	60	70	51	56	50
10	105	122	124	66	49	46
Mean (SD)	81 (30)	89 (28)	98 (33)	90 (41)	84 (34)	82 (45)

Table 4-24: The differences in the stepping time for all participants for both groups.

Subject	Differences in stepping time (min/day)			
	LWI Group		Neutral Insole Group	
	W1-Baseline	W6-Baseline	W1-Baseline	W6-Baseline
1	23	24	-9	-14
2	0	31	12	-3
3	4	25	-14	-9
4	-16	-7	-33	7
5	6	22	0	-24
6	6	23	4	2
7	37	22	1	19
8	2	0	-10	-33
9	0	10	5	-1
10	17	19	-17	-20
Mean	8	17	-6	-8

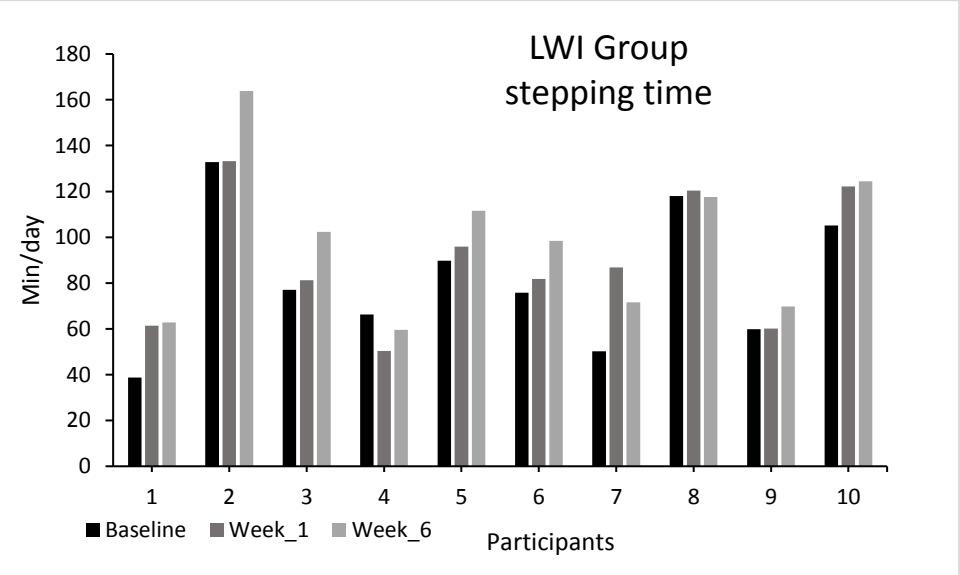

Figure 4-17: The mean of stepping time for all participants for baseline, week 1, and week 6 in LWI group.

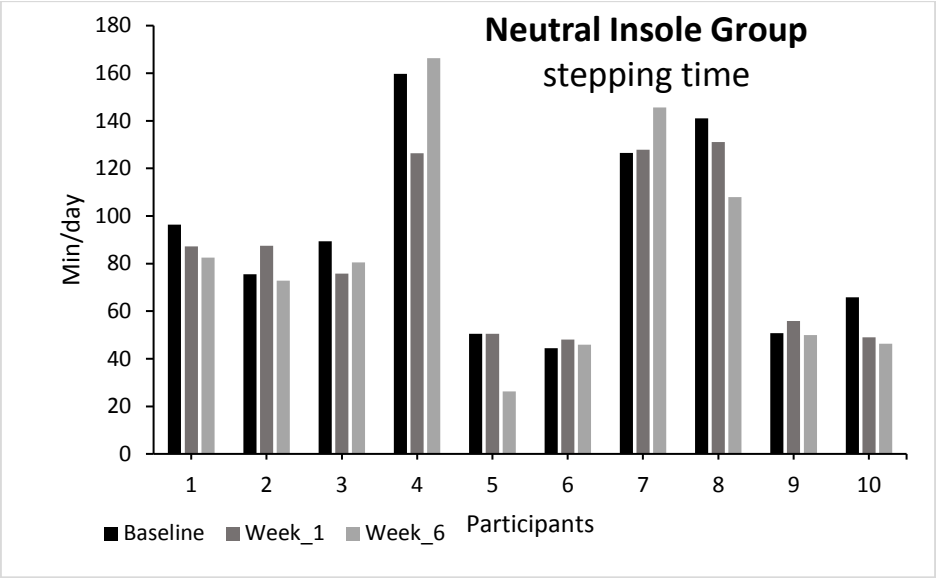

Figure 4-18: The mean of stepping time for all participants for baseline, week 1, and week 6 in neutral insole group.

4.10.5.5. Standing time

The mean, SD, mean difference, and changes in the standing time per day for both groups are shown in table 4-25 and table 4-26. Table 4-27 and figures 4-19 & 4-20 show the average of standing time for all participants at baseline, week one, and week six for both groups (LWI group and neutral insole group). The groups (LWI and comparator groups) had no statistically significant effect on the average of standing time (p=0.712). The main effect of duration of intervention "weeks" (baseline, week one, and week six) had no significant effect on the standing time (p=0.486) and there was no significant interaction between the groups and weeks (p=0.530).

After wearing LWIs for one week, the average of standing time did not change significantly (mean difference 1 min/day, p=0.941) in comparison to baseline, although the standing time increased slightly (average increase was 0.5%, range -27%-25%). After wearing LWIs for six weeks, the standing time did not change significantly (mean difference 18 min/day, p=0.141) in comparison to baseline, although the standing time increased slightly (average increase was 9.1%, range -51%-87%).

After wearing neutral insole for one week, the average of standing time did not change significantly (mean difference 20 min/day, p=0.479) in comparison to baseline, although the standing time increased slightly (average increase was 10.7%, range -40%-34%). After wearing neutral insole for six weeks, the standing time did not change significantly (mean difference 11 min/day, p=0.675) in

comparison to baseline, although the standing time increased slightly (average increase was 5.7%, range -66%-69%).

There was no significant difference in the changes between baseline compared to week one or week six between LWI group and comparator group.

Table 4-25: Mean (SD), and mean differences of the standing time for groups

	Mean (SD)						Mean difference within groups			
	Week 0		Week 1		Week 6		week 0 vs. Week 1		week 0 vs. Week 6	
	LWI	Neutral	LWI	Neutral	LWI	Neutral	LWI	Neutral	LWI	Neutral
standing time (min/day)	203 (84)	188 (43)	204 (69)	208 (59)	221 (77)	199 (95)	1 0.941	20 0.479	18 0.141	11 0.675

Table 4-26: The mean of the standing time (min/day) for individuals

Subject	LWI Group			Neutral Insole Group		
	Baseline	Week 1	Week 6	Baseline	Week 1	Week 6
1	196	237	202	133	145	110
2	238	281	320	182	190	129
3	226	260	323	262	286	372
4	103	128	192	183	202	189
5	255	204	220	223	233	75
6	299	218	146	200	267	299
7	75	84	90	130	175	221
8	226	244	262	229	286	266
9	98	119	168	149	186	214
10	309	260	287	188	113	113
Mean (SD)	203 (84)	204 (69)	221 (77)	188 (43)	208 (59)	199 (95)

Table 4-27: The differences in the standing time for all participants for both groups.

Subject	Differences in standing time (min/day)			
	LWI Group		Neutral Insole Group	
	W1-Baseline	W6-Baseline	W1-Baseline	W6-Baseline
1	41	6	12	-23
2	43	82	8	-53
3	34	98	24	110
4	26	89	19	6
5	-52	-35	10	-148
6	-81	-153	67	99
7	9	15	45	91
8	18	36	57	37
9	21	70	37	65
10	-49	-22	-75	-75
Mean	1	18.4	20.4	10.9

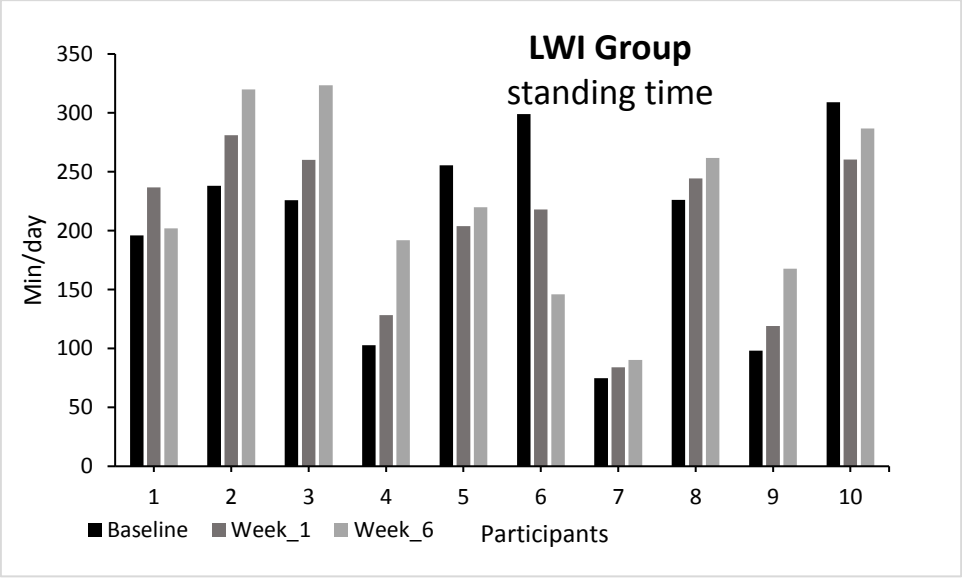

Figure 4-19: The mean of standing time for all participants for baseline, week 1, and week 6 in LWI group.

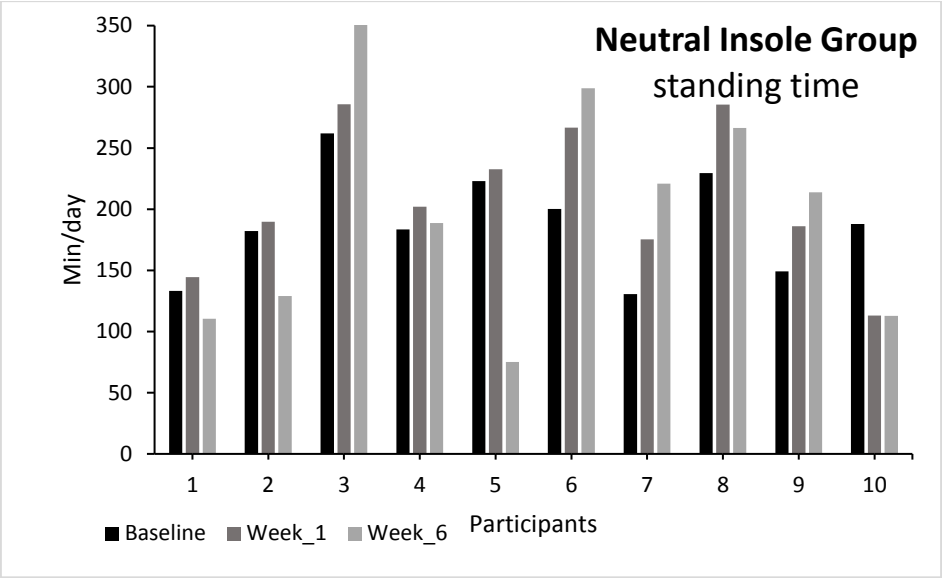

Figure 4-20: The mean of standing time for all participants for baseline, week 1, and week 6 in neutral insole group.

4.10.6. Walking pattern

4.10.6.1. Length of walking

The mean minutes per day of length of walking across different walking bands for baseline, week one and week six for both lateral wedged insole and comparator groups is shown in table 4-28, figure 4-21 and figure 4-22.

The continuous walking time in the 5-10 min band increased in LWI group in week one and week six compared to baseline. The results showed that the LWI group walked for a longer time in the 5-10 minute walking band when wearing LWI for one and six weeks compared to baseline. Individuals with LWI walked for a longer period, whereas the comparator group shows no change in term walking length.

Table 4-28: Length of walking (mean minutes per day) across different walking bands (in minute) for baseline, week 1 and week 6 for lateral wedged insole group and neutral insole group.

Walking band	LWI0	LWI1	LWI6	Walking band	N0	N1	N6
0-0.5	35.4	38.3	38.6	0-0.5	35	35.9	36.2
0.5-1	11	11.7	12.2	0.5-1	13.8	13.4	13.3
1-2	6.9	6.7	9.0	1-2	9.0	9.9	8.3
2-3	3.9	4.9	4.9	2-3	6.8	6.0	5.3
3-4	4.2	5.5	5.8	3-4	4.5	4.1	4.5
4-5	3.4	4.8	4.8	4-5	1.9	2.4	2.7
5-10	8.3	12.5	15.1	5-10	9.6	7.9	7.5
10-20	4.3	4.6	5.4	10-20	7.2	2.3	3.8
20-30	2.1	0.4	1.0	20-30	1.6	0.3	0.0
>30	1.8	0.0	1.4	>30	0.0	0.0	0.0
SUM	81.3	89.3	98.2	SUM	89.4	82.1	81.7

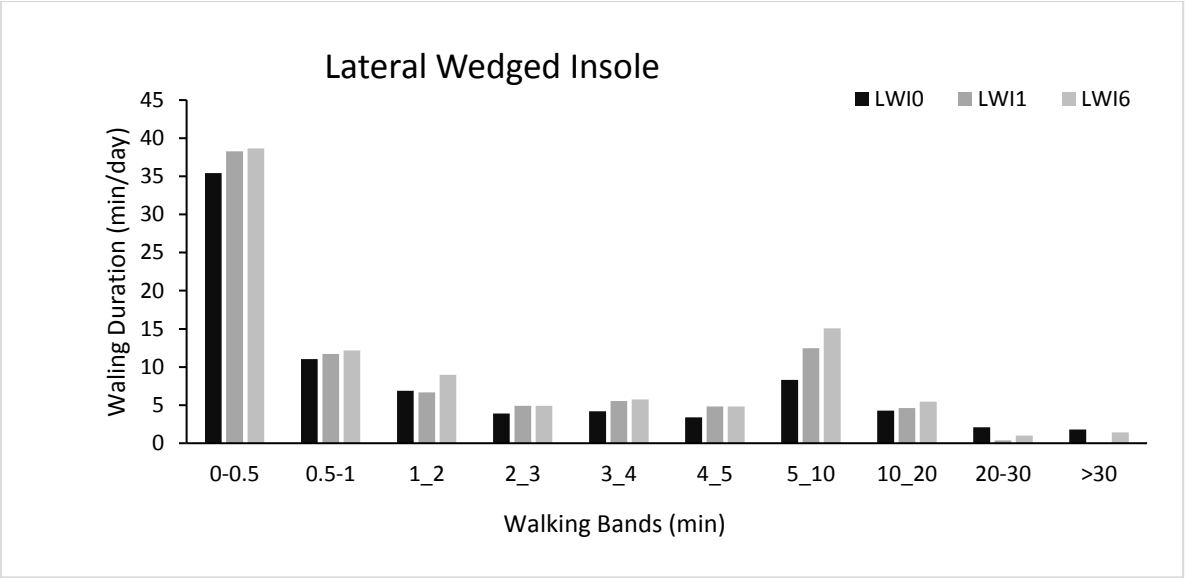

Figure 4-21: Mean minutes per day of length of walking (duration) across different walking bands for baseline, week 1 and week 6 for lateral wedged insole group.

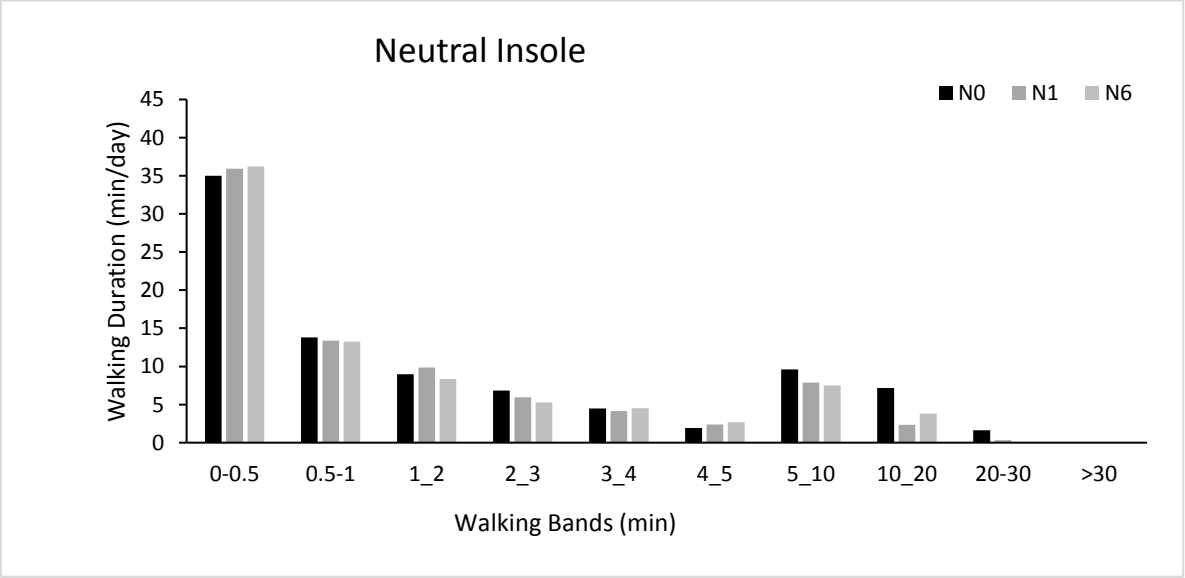

Figure 4-22: Mean minutes per day of length of walking (duration) across different walking bands for baseline, week 1 and week 6 for neutral insole group.

4.10.6.2. Cadence

The mean minutes per day across cadence bands for baseline, week one and week six for both lateral insole and comparator groups is shown in table 4-29, figure 4-23 and figure 4-24.

The main difference in LWI group was in the cadence bands from 90 to 110 steps/minutes, the LWI group showed an increase in the amount of time walking per day at these cadences whereas the comparator group showed no change at any cadence band.

Table 4-29: Mean minutes per day across cadence bands (steps/day) for baseline, week 1 and week 6 for both lateral insole and neutral insole groups.

Cadence band	LWI0	LWI1	LWI6	Cadence band	N0	N1	N6
≤10	0.0	0.0	0.0	≤10	0.0	0.0	0.0
10-20	0.0	0.0	0.0	10-20	0.0	0.0	0.0
20-30	2.58	2.90	2.90	20-30	2.25	2.68	2.43
30-40	4.10	4.13	4.28	30-40	3.73	4.09	4.18
40-50	6.37	6.70	6.51	40-50	7.31	7.28	8.53
50-60	8.72	9.53	8.90	50-60	13.30	12.42	12.11
60-70	8.99	9.96	9.86	60-70	12.83	12.89	10.85
70-80	9.25	9.80	10.09	70-80	10.47	11.13	10.40
80-90	7.83	10.50	9.95	80-90	9.48	9.61	8.91
90-100	12.54	14.46	18.35	90-100	11.55	11.07	10.18
100-110	14.35	16.32	22.10	100-110	7.45	6.63	5.82
110-120	3.95	3.55	3.98	110-120	5.42	3.48	4.77
120-130	2.49	1.32	1.02	120-130	4.43	0.63	3.34
130-140	0.07	0.06	0.18	130-140	1.11	0.10	0.10
140-150	0.05	0.04	0.05	140-150	0.03	0.07	0.03
150-160	0.0	0.01	0.01	150-160	0.0	0.01	0.01
160-170	0.0	0.0	0.0	160-170	0.0	0.0	0.0
170-180	0.02	0.02	0.02	170-180	0.02	0.02	0.02
SUM	81.33	89.31	98.19	**SUM**	89.38	82.11	81.67

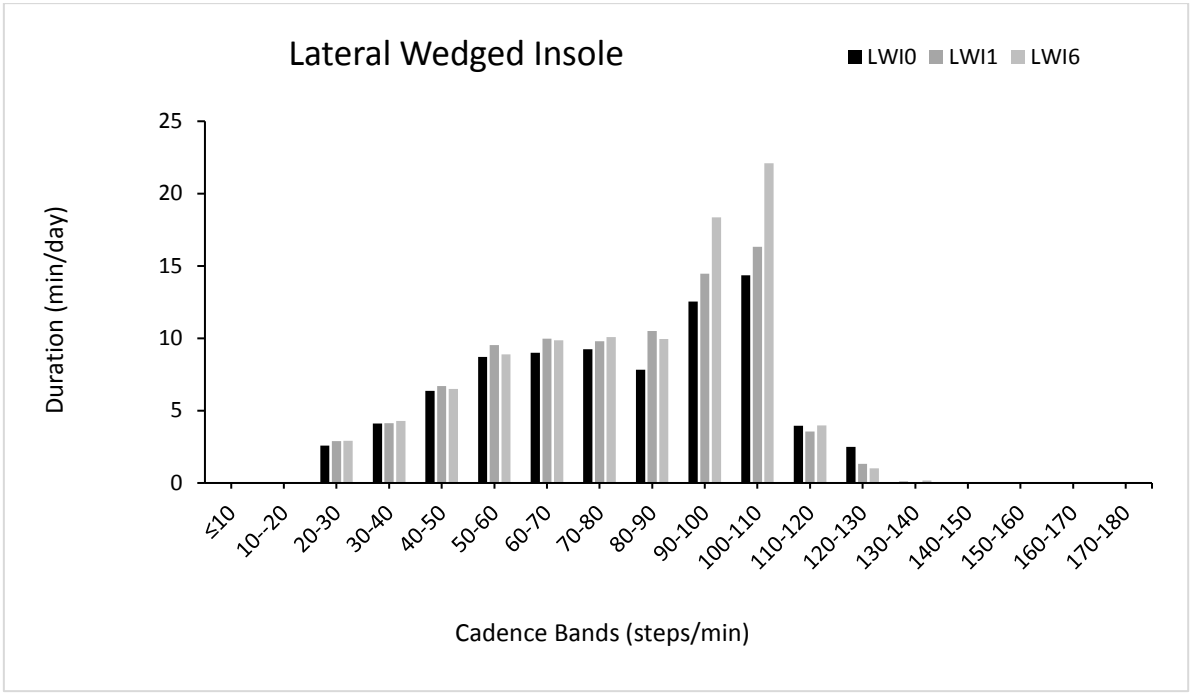

Figure 4-23: Mean minutes per day across cadence bands for baseline, week 1 and week 6 for lateral wedge insole group.

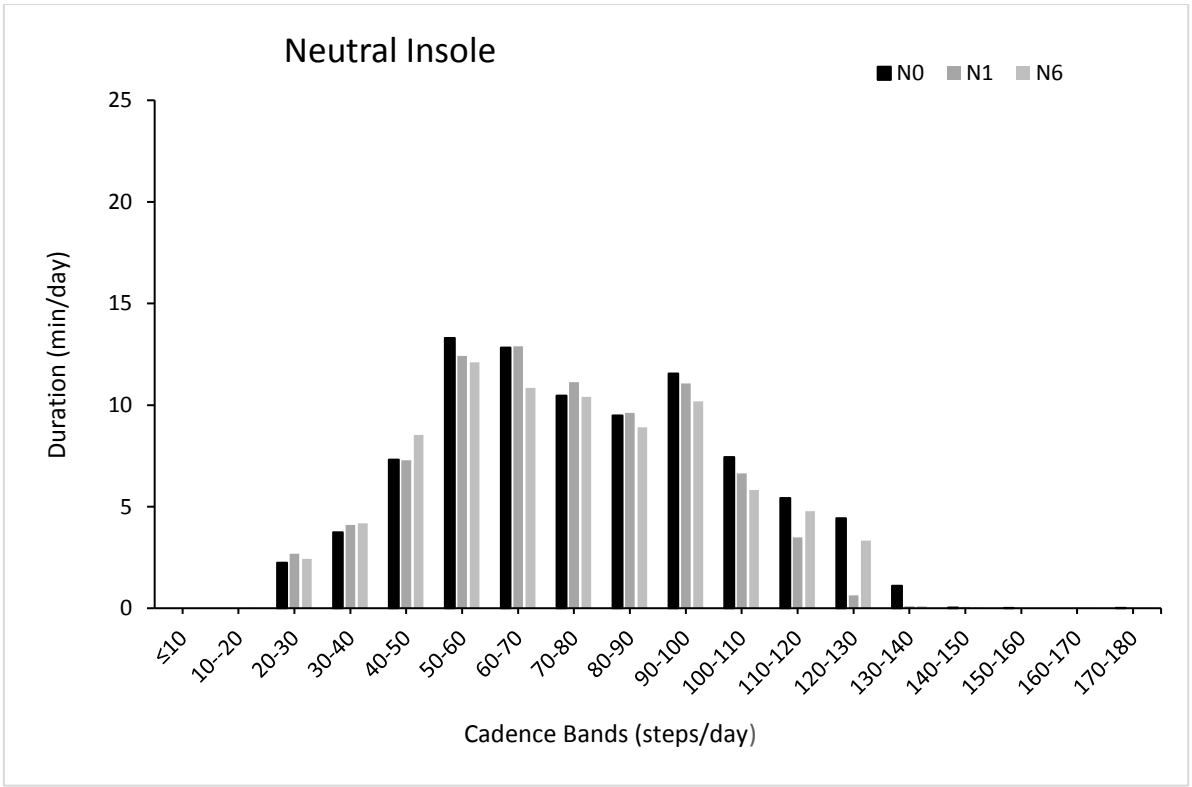

Figure 4-24: Mean minutes per day across cadence bands for baseline, week 1 and week 6 for neutral insole group.

4.10.7. Knee injury and Osteoarthritis Outcome Score (KOOS) results

Knee pain was measured pre-, during, and after 6 weeks of wearing the LWI insoles and neutral insoles. Mean (SD) of knee pain with the mean difference for both groups is presented in Table 4-30. Knee pain was significantly improved after wearing either LWI or neutral insole for one or six weeks compared to baseline with no significant differences between groups ($p \geq 0.05$).

Table 4-30: Mean, standard deviation (SD), mean differences and p-value of the knee pain (KOOS) for both groups.

	Mean (SD)						Mean difference within groups (p-value)			
	Week 0		Week 1		Week 6		week 0 vs. week 1		week 0 vs. week- 6	
	LWI	Neutral	LWI	Neutral	LWI	Neutral	LWI	neutral	LWI	Neutral
KOOS (pain scale)	51.9 (15.55)	49.8 (11.7)	66.5 (15.97)	67.6 (11.64)	65 (11.2)	61.1 (8.83)	-14.6 **0.013***	-17.8 **0.004***	-13.1 **0.003***	-11.3 **0.01***

*Significant difference value

4.10.8. Kinematics results over one week for the two groups

4.10.8.1. Temporal and spatial data for the two groups

The ANOVA analysis has showed that there was no significant difference between groups ($p \geq 0.05$) with a significant interaction between groups and weeks on the speed ($p=0.03$) and cadence ($p=0.02$). The main effect of weeks (time) was significant on all temporal and spatial variables ($p=0.00$). The descriptive data is presented in table 4-31.

After wearing LWI for one week, all variables were significantly increased (except stance time decreased significantly) compared to baseline ($p<0.05$). Speed was increased significantly by 17% (mean difference 0.15 m/s (0.07), $p=0.000$) in week one compared to baseline.

After wearing neutral insole for one week, all variables were significantly increased compared to baseline ($p<0.05$) except stance time (affected and unaffected sides) and cadence did not change significantly; $p=0.12$, $p=0.18$ and $p=0.13$, respectively. Speed was increased significantly by 11.9 % (mean difference 0.10 m/s (0.07), $p=0.004$) compared to baseline. After one week, cadence was increased significantly in wedged group compared to comparator group ($p=0.002$). Walking speed increased after wearing LWI for one week compared to comparator group but not significant.

Table 4-31: Mean (SD) temporal and spatial variables for two groups after wearing insoles for one week.

	Mean (SD)							
	Baseline				Week One			
	Wedged Group		Neutral Group		Wedged Group		Neutral Group	
	Shod	LWI	Shod	Neutral insole	Shod	LWI	Shod	Neutral insole
Speed (m/s)	0.9 (0.2)	0.9 (0.2)	0.8 (0.2)	0.9 (0.2)	0.9 (0.2)	1.0* (0.2)	0.9 (0.2)	0.9* (0.3)
Stride Length (m)	1.2 (0.2)	1.2 (0.2)	1.2 (0.2)	1.2 (0.2)	1.3 (0.2)	1.4* (0.1)	1.3 (0.1)	1.4* (0.1)
Affected step length(m)	0.6 (0.1)	0.6 (0.1)	0.6 (0.1)	0.6 (0.1)	0.7 (0.1)	0.7* (0.1)	0.7 (0.1)	0.7* (0.0)
Unaffected step length(m)	0.6 (0.1)	0.6 (0.1)	0.6 (0.1)	0.6 (0.1)	0.6 (0.1)	0.7* (0.1)	0.6 (0.1)	0.6* (0.1)
Affected stance time (s)	0.9 (0.1)	0.9 (0.1)	1.0 (0.2)	1.0 (0.2)	0.9 (0.1)	0.9* (0.1)	1.0 (0.2)	0.9 (0.3)
Unaffected stance time(s)	0.9 (0.1)	0.9 (0.1)	1.0 (0.3)	1.0 (0.2)	0.9 (.1)	0.9* (0.1)	1.0 (0.3)	1.0 (0.3)
Cadence (step/min)	82.9 (9.9)	85.9 (11.6)	80.7 (14.9)	84.5 (18.6)	83.8 (13.2)	90.1* (11.1)	81.0 (18.0)	84.2 (18.5)

*Significant difference value compared to baseline.

4.10.8.2. Hip angle in sagittal plane for the two groups

There was no significant difference between groups or weeks ($p \geq 0.05$) and the ANOVA analysis has also showed that there is no significant interaction between groups and weeks ($p \geq 0.05$) on the maximum hip extension, the maximum hip flexion angle, and the hip ROM. The descriptive data is presented in Table 4-32. The data from baseline and week one indicated that LWI and neutral insole did not significantly change the maximum hip extension angle, the maximum hip flexion angle and the hip ROM compared to baseline and comparator group (Figure 4-25).

Table 4-32: Mean (SD) hip angle in sagittal plane during walking for two groups after wearing insoles for one week.

Hip angle (degree)	Mean (SD)							
	Baseline (week 0)				Week One			
	Wedged Group		Neutral Group		Wedged Group		Neutral Group	
	Shod	LWI	Shod	Neutral insole	Shod	LWI	Shod	Neutral insole
Maximum hip extension	-6.3 (7.4)	-5.3 (7.2)	-5.5 (10.1)	-6.0 (10.2)	-7.8 (6.0)	-7.2 (5.7)	-7.3 (6.7)	-7.3 (7.2)
Maximum hip flexion	30 (4.4)	31.3 (5.7)	30.1 (5.4)	30.6 (5.2)	28.5 (6.8)	29.8 (7.7)	28 (5.0)	28.4 (4.2)
Hip ROM (degree)	36.3 (7.80)	36.6 (7.0)	35.6 (7.2)	36.6 (7.2)	36.3 (6.3)	37 (6.1)	35.3 (6.9)	35.8 (6.0)

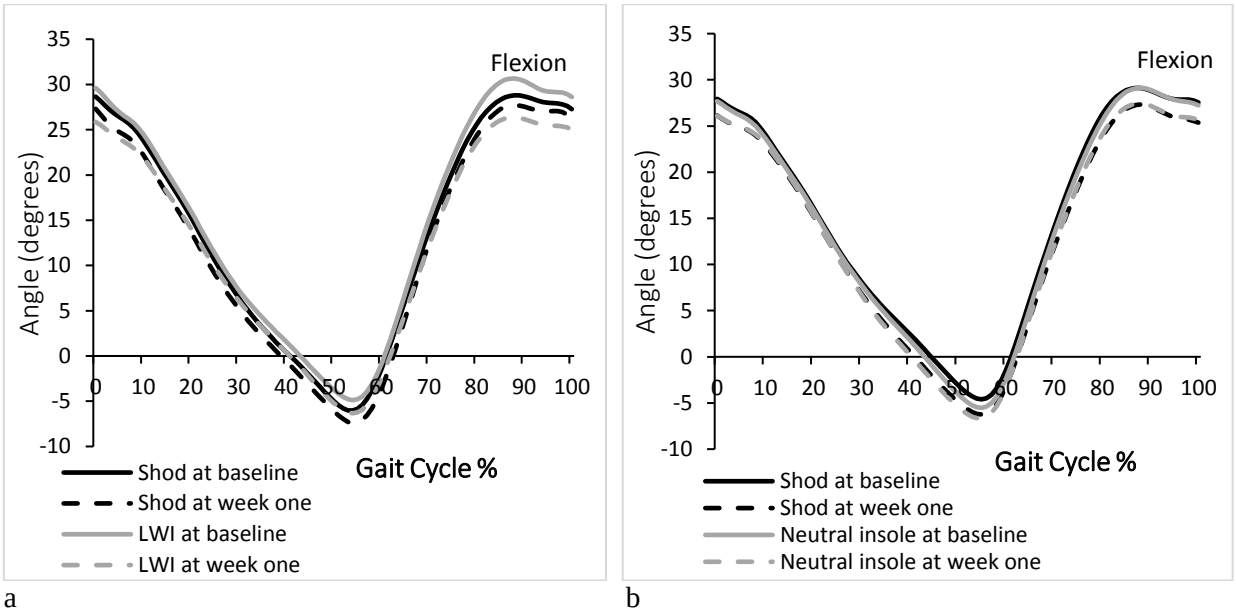

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Figure 4-25: The hip angle in sagittal plane for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.8.3. Knee angle in sagittal plane for the two groups

There groups or weeks had no significant effect ($p \geq 0.05$) and the ANOVA analysis has also showed that there was no significant interaction between groups and weeks ($p \geq 0.05$) on the knee flexion angle at initial contact, the maximum knee angle at loading response, the knee extension angle at mid stance, the maximum knee flexion angle at mid-swing and the sagittal knee ROM. Whereas, the effect of weeks on the knee ROM in sagittal plane was significant ($p < 0.05$). The descriptive data is presented in table 4-33.

The data from baseline and week one indicated that LWI and neutral insoles did not significantly change the maximum knee flexion angle at initial contact, the maximum knee flexion angle at loading response, the knee extension angle at mid stance, the maximum knee flexion angle at mid swing and the sagittal knee ROM in comparison to baseline and comparator group (Figure 4-26). Whereas, there was a significant increase in the maximum knee flexion angle at loading response (mean difference 1.89(2.5) degree, p=0.043), the maximum knee flexion angle at mid swing (mean difference 2.03(2.0) degree, p=0.01) and the knee ROM in sagittal plane (mean difference 1.4(1.6) degree, p=0.02) after wearing LWI for one week in comparison to the shod only at week one.

Table 4-33: Mean (SD) knee angle in sagittal plane during walking for two groups after wearing insoles for one week.

Knee angle (degree)	Mean (SD)							
	Baseline (week 0)				Week One			
	Wedged Group		Neutral Group		Wedged Group		Neutral Group	
	Shod	LWI	Shod	Neutral insole	Shod	LWI	Shod	Neutral insole
Initial contact	0.47 (5.7)	0.89 (5.5)	2.07 (6.2)	1.55 (7.1)	0.48 (5.3)	0.16 (5.4)	0.59 (8.8)	0.10 (9.8)
Loading response (peak knee flexion)	8.26 (7.6)	9.25 (7.5)	10.72 (6.8)	11.11 (7.9)	8.0 (7.5)	9.90* (7.9)	10.47 (9.3)	10.42 (10.0)
Mid-stance (knee extension)	2.93 (7.1)	3.48 (6.9)	5.53 (7.0)	5.12 (7.6)	2.89 (6.7)	3.51 (6.7)	3.95 (9.2)	3.61 (9.6)
Mid-swing (peak knee flexion)	56.99 (7.1)	58.7 (7.6)	57.68 (6.7)	58.30 (6.5)	56.98 (9.1)	58.9* (8.5)	54.77 (8.8)	55.94 (8.3)
Knee ROM (degree)	54.1 (9.4)	55.2 (9.4)	52.15 (11.7)	53.18 (12.2)	54.0 (9.1)	55.4* (8.9)	50.83 (12.0)	52.33 (11.8)

*Significant difference value compared to baseline at week one

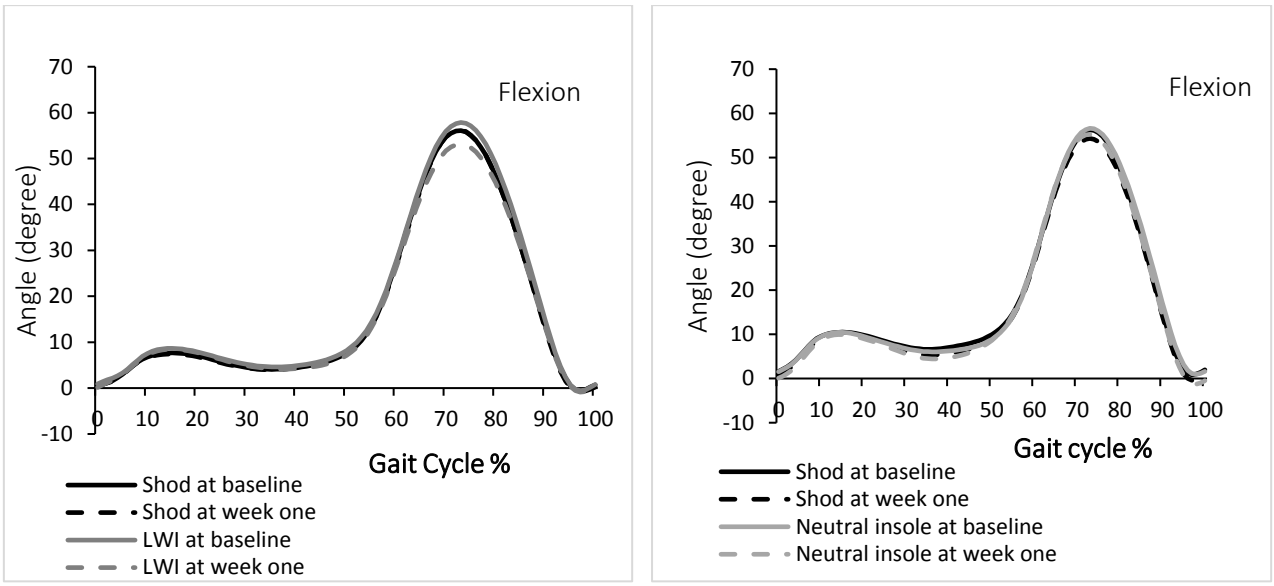

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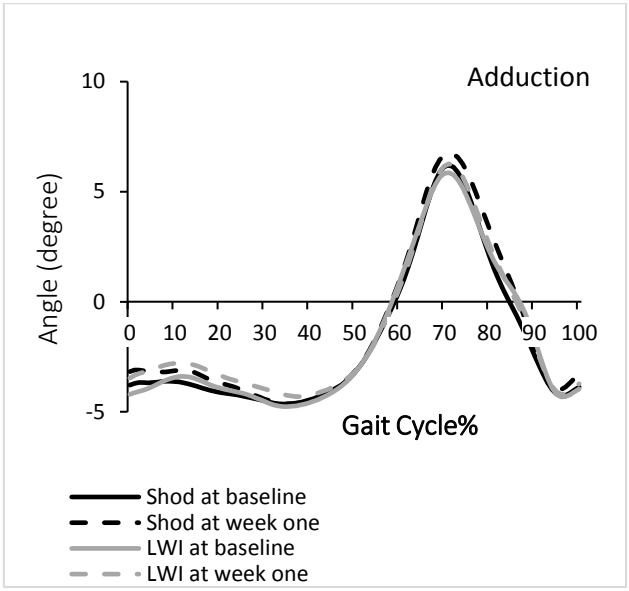
Figure 4-26: The knee angle in sagittal plane for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.8.4. Knee angle in frontal plane for the two groups

There was no significant difference between groups or weeks ($p \geq 0.05$) and the ANOVA analysis has also showed that there is no significant interaction between groups and weeks ($p \geq 0.05$) on the maximum knee adduction angle, the maximum knee abduction angle and the knee ROM in frontal plane. The descriptive data is presented in table 4-34. The data from baseline and week one indicated that LWI did not significantly change the maximum knee adduction angle, the maximum knee abduction angle and the knee ROM in frontal plane in comparison to baseline and comparator group (Figure 4-27).

Table 4-34: Mean (SD) knee angle in frontal plane during walking for two groups after wearing insoles for one week.

Knee angle	Mean (SD)							
	Baseline (week 0)				Week One			
	Wedged Group		Neutral Group		Wedged Group		Neutral Group	
	Shod	LWI	Shod	Neutral insole	Shod	LWI	Shod	Neutral insole
Maximum knee adduction (degree)	7.96 (6.2)	8.50 (5.8)	8.88 (4.6)	9.01 (4.5)	8.89 (5.9)	8.63 (6.6)	9.55 (5.0)	9.75 (5.0)
Maximum knee abduction (degree)	-6.53 (3.2)	-6.83 (3.0)	-4.56 (3.2)	-4.74 (3.8)	-6.21 (2.4)	-6.61 (2.6)	-5.33 (2.2)	-5.25 (2.8)
Knee ROM (degree)	14.49 (6.3)	15.33 (6.1)	13.45 (5.8)	13.75 (5.7)	15.10 (6.4)	15.23 (6.8)	14.88 (4.9)	15 (4.9)



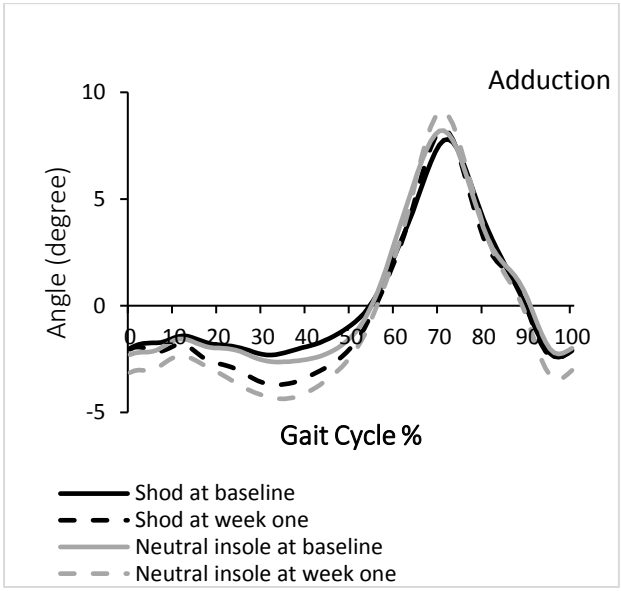


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Figure 4-27: The knee angle in frontal plane for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.8.5. Ankle angle in sagittal plane for the two groups

There was no significant difference between groups ($p \geq 0.05$) and the ANOVA analysis has also showed that there is no significant interaction between groups and weeks ($p \geq 0.05$) on the ankle dorsiflexion angle, the ankle plantar-flexion angle and the ankle ROM in sagittal plane. Whereas, the effect of weeks on ankle dorsiflexion angle, the ankle ROM in sagittal plane was significant ($p < 0.05$). The descriptive data is presented in table 4-35.

The data from baseline and week one indicated that LWI and neutral insoles did not significantly change the ankle dorsiflexion angle and the ankle plantar-flexion angle and the ankle ROM in sagittal plane in comparison to baseline and comparator group. Whereas, the ankle ROM in sagittal plane significantly increased (mean difference 2.15(2.9) degree, p=0.015) after wearing LWI for one week in comparison to the shod at baseline (Figure 4-28).

Table 4-35: Mean (SD) ankle angle in sagittal plane during walking for two groups after wearing insoles for one week.

Ankle angle	Mean (SD)							
	Baseline (week 0)				Week One			
	Wedged Group		Neutral Group		Wedged Group		Neutral Group	
	Shod	LWI	Shod	Neutral insole	Shod	LWI	Shod	Neutral insole
Ankle dorsiflexion (degree)	20.16 (3.9)	21.43 (4.0)	22.12 (3.3)	22.48 (3.3)	21 (3.5)	21.03 (3.5)	21.69 (4.5)	22.12 (5.1)
Ankle plantar-flexion (degree)	-6.44 (6.1)	-5.35 (5.6)	-5.38 (5.0)	-5.51 (5.7)	-6.02 (6.1)	-7.72 (6.0)	-5.41 (5.8)	-5.66 (5.8)
Ankle ROM (degree)	26.60 (5.3)	26.78 (4.7)	27.51 (3.5)	27.99 (3.4)	27.02 (5.4)	28.75* (5.4)	27.10 (4.3)	27.79 (3.4)

***** Significant difference compared to baseline

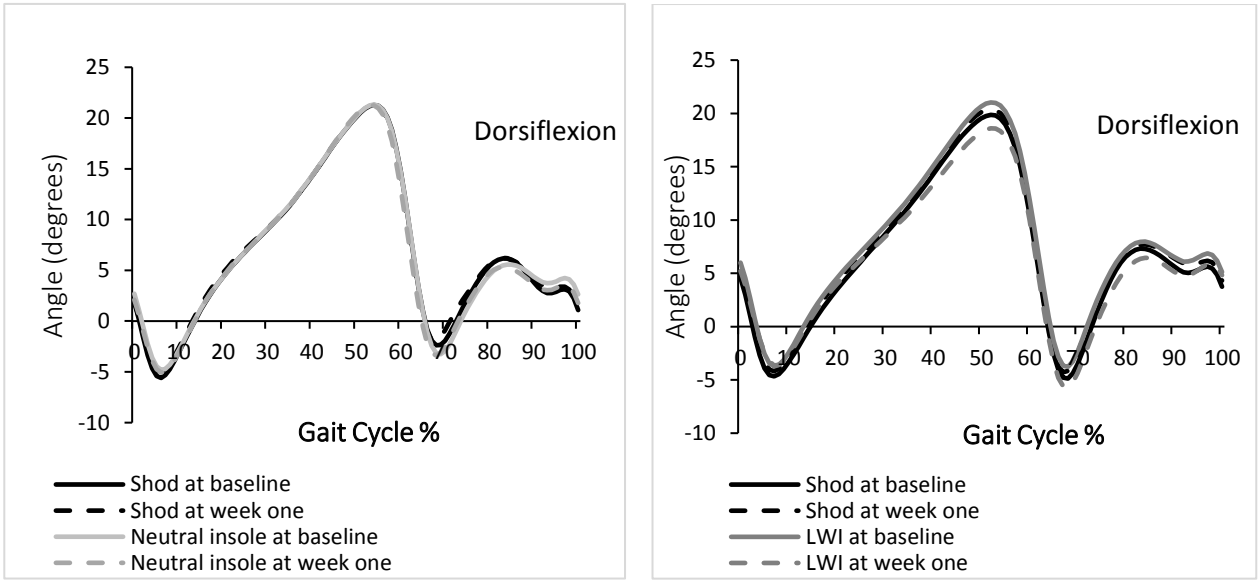

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Figure 4-28: The ankle angle in sagittal plane for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.9. Kinematics results over six weeks for the two groups

4.10.9.1. Temporal and spatial data for the two groups

The ANOVA analysis has showed that there was no significant difference between groups ($p \geq 0.05$) with a significant interaction between groups and weeks on the speed ($p=0.03$) and cadence (0.02). The main effect of weeks (time) was significant on all temporal and spatial variables ($p=0.00$). The descriptive data is presented in table 4-36.

After wearing LWI for six weeks, all variables were significantly increased compared to baseline ($p<0.05$) except stance time significantly reduced ($p<0.05$) and unaffected step length did not change significantly $p \geq 0.05$). Speed was significantly increased by 19% (mean difference 0.16 m/s (0.08), $p=0.00$) compared to baseline.

After wearing neutral insole for six weeks, all variables were increased significantly (except stance time did not change) compared to baseline ($p<0.05$). Speed was increased significantly by 10.2 % (mean difference 0.09 m/s (0.07), $p=0.004$) compared to baseline. There was no significant difference between groups in all temporal and spatial variables after wearing insoles (either LWI or neutral insole).

Table 3-36: Mean (SD) temporal and spatial variables for two groups after wearing insoles for six weeks.

	Mean (SD)					
	Baseline		Week Six			
			Wedged Group		Neutral Group	
	Wedged Group	Neutral Group	Shod	LWI	Shod	Neutral insole
Speed (m/s)	0.9 (0.2)	0.8 (0.2)	1.0 (0.2)	1.0* (0.2)	0.9 (0.3)	0.9* (0.2)
Stride Length (m)	1.2 (0.2)	1.2 (0.2)	1.2 (0.2)	1.3* (0.2)	1.3 (0.2)	1.3* (0.2)
Affected step length(m)	0.6 (0.1)	0.6 (0.1)	0.6 (0.1)	0.7* (0.1)	0.6 (0.1)	0.6* (0.1)
Unaffected step length(m)	0.6 (0.1)	0.6 (0.1)	0.7 (0.1)	0.7 (0.1)	0.6 (0.1)	0.6 (0.1)*
Affected stance time (s)	0.9 (0.1)	1.0 (0.2)	0.8 (0.1)	0.8* (0.1)	1.0 (0.3)	0.9 (0.2)
Unaffected stance time(s)	0.9 (0.1)	1.0 (0.3)	0.9 (0.1)	0.8* (0.1)	1.0 (0.3)	0.9 (0.2)
Cadence (step/min)	82.9 (9.9)	80.7 (14.9)	90.0 (10.4)	94.5* (9.4)	81.2 (15.8)	84.2* (14.5)

*Significant difference value compared to baseline.

4.10.9.2. Hip angle in sagittal plane for the two groups

There was no significant difference between groups or weeks ($p \geq 0.05$) and the ANOVA analysis has also showed that there is no significant interaction between groups and weeks ($p \geq 0.05$) on the maximum hip extension, the maximum hip flexion angle, and the hip ROM in sagittal plane. The descriptive data is presented in table 4-37.

The data from baseline and week six indicated that LWI and neutral insole did not significantly change the maximum hip extension angle, the maximum hip flexion angle and the hip ROM in sagittal plane compared to baseline and comparator group (Figure 4-29).

Table 4-37: Mean (SD) hip angle in sagittal plane during walking for two groups after wearing insoles for six weeks.

Hip angle (degree)	Mean (SD)					
	Baseline (week 0)		Week Six			
	Wedged Group	Neutral Group	Wedged Group		Neutral Group	
			Shod	LWI	Shod	Neutral insole
Max hip extension (late stance)	-6.3 (7.4)	-5.5 (10.1)	-5.8 (5.9)	-6.1 (6.5)	-7.6 (7.8)	-7.9 (7.8)
Max hip flexion (swing phase)	30. (4.4)	30.1 (5.4)	31 (3.9)	31.6 (4.2)	27.8 (5.5)	28.1 (4.7)
Hip ROM (degree)	36.3 (7.80)	35.6 (7.2)	36.8 (7.4)	37.7 (7.8)	35.4 (7.4)	36 (7.2)

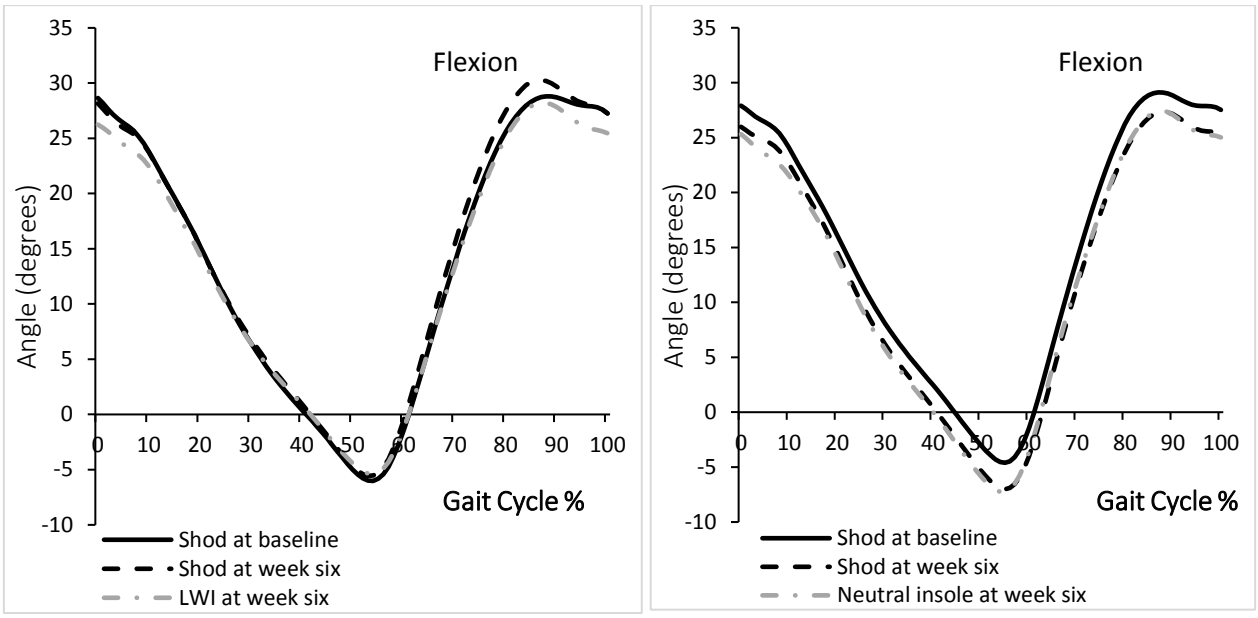

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Figure 4-29: The hip angle in sagittal plane for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.9.3. Knee angle in sagittal plane for the two groups

There groups or weeks had no significant effect ($p \geq 0.05$) and the ANOVA analysis has also showed that there was no significant interaction between groups and weeks ($p \geq 0.05$) on the knee flexion angle at initial contact, the maximum knee angle at loading response, the knee extension angle at mid stance, the maximum knee flexion angle at mid-swing and the sagittal knee ROM. Whereas, the effect of weeks on the knee ROM in sagittal plane was significant ($p < 0.05$). The descriptive data is presented in table 4-38.

The data from baseline and week six indicated that LWI and neutral insole did not significantly change the knee flexion angle at initial contact, the maximum knee flexion angle at loading response, the knee extension angle at mid stance, the maximum knee flexion angle at mid swing and the sagittal knee ROM in comparison to baseline and comparator group. Whereas, after wearing LWI for six weeks, the ROM knee ROM knee in sagittal plane significantly increased (mean difference 2.4(3.8) degree, p=0.049) in comparison to the shod at baseline (Figure 4-30).

Table 4-38: Mean (SD) knee angle in sagittal plane during walking for two groups after wearing insoles for six weeks.

Knee angle (degree)	Mean (SD)					
	Baseline (week 0)		Week Six			
	Wedged Group	Neutral Group	Wedged Group		Neutral Group	
			Shod	LWI	Shod	Neutral insole
Initial contact	0.47 (5.7)	2.07 (6.2)	0.50 (6.8)	0.02 (6.9)	2.31 (6.9)	2.11 (6.5)
Loading response (peak knee flexion)	8.26 (7.6)	10.72 (6.8)	9.46 (7.4)	10.54 (8.2)	11.70 (8.1)	12.24 (7.2)
Mid-stance (knee extension)	2.93 (7.1)	5.53 (7.0)	4.10 (6.8)	3.73 (7.1)	6.01 (7.3)	6.30 (6.50)
Mid-swing (peak knee flexion)	56.99 (7.1)	57.68 (6.7)	59.38 (8.7)	56.46 (15.1)	57.7 (6.2)	58.78 (6.4)
Knee ROM (degree)	54.1 (9.4)	52.15 (11.7)	55.28 (8,8)	56.40* (8.8)	51.72 (11.1)	52.48 (10.6)

***** Significant difference compared to baseline

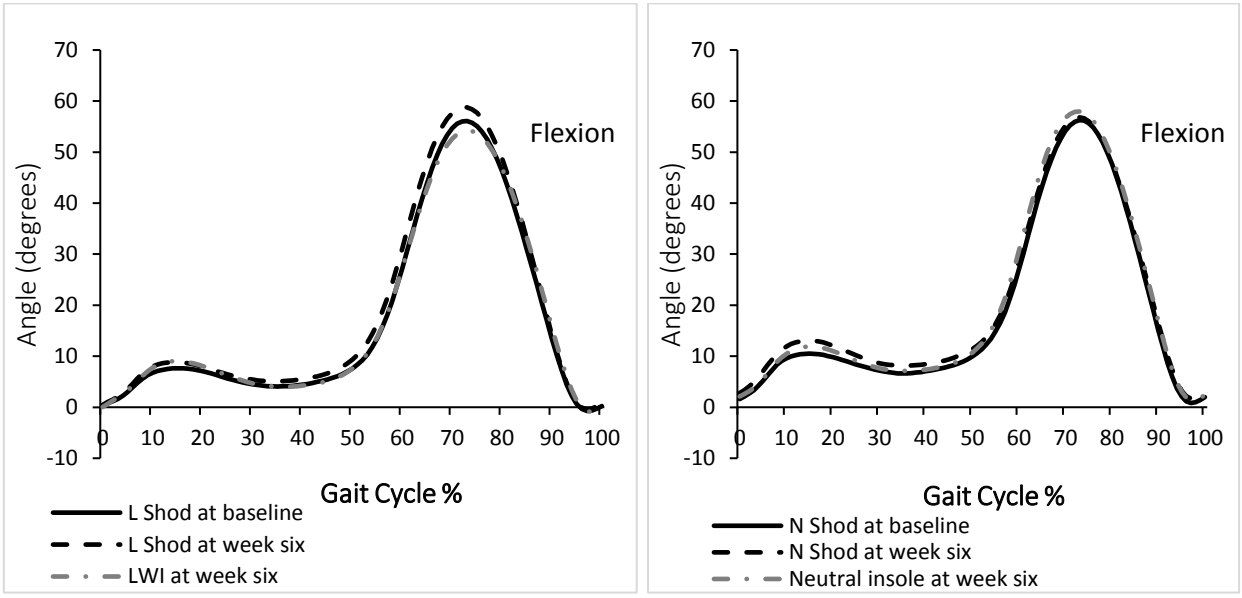

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Figure 4-30: The knee angle in sagittal plane for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.9.4. Knee angle in frontal plane for the two groups

There was no significant difference between groups or weeks ($p \geq 0.05$) and the ANOVA analysis has also showed that there is no significant interaction between groups and weeks ($p \geq 0.05$) on the maximum knee adduction angle, the maximum knee abduction angle and the knee ROM in frontal plane. The descriptive data is presented in table 4-39. The data from baseline and week six indicated that LWI did not significantly change the maximum knee adduction angle, the maximum knee abduction angle and the frontal knee ROM in comparison to baseline and comparator group (Figure 4-31).

Table 4-39: Mean (SD) knee angle in frontal plane during walking for two groups after wearing insoles for six weeks.

Knee angle (degree)	Mean (SD)					
	Baseline (week 0)		Week Six			
	Wedged Group	Neutral Group	Wedged Group		Neutral Group	
			Shod	LWI	Shod	Neutral insole
Maximum knee adduction	7.96 (6.2)	8.88 (4.6)	8.77 (5.3)	8.44 (5.4)	10.24 (3.2)	11.12 (3.8)
Maximum knee abduction	-6.53 (3.2)	-4.56 (3.2)	-6.34 (4.0)	-6.04 (3.8)	-4.44 (3.3)	-4.04 (2.7)
Knee ROM (degree)	14.49 (6.3)	13.45 (5.8)	15.12 (4.0)	14.49 (3.6)	14.68 (4.5)	14.85 (4.6)

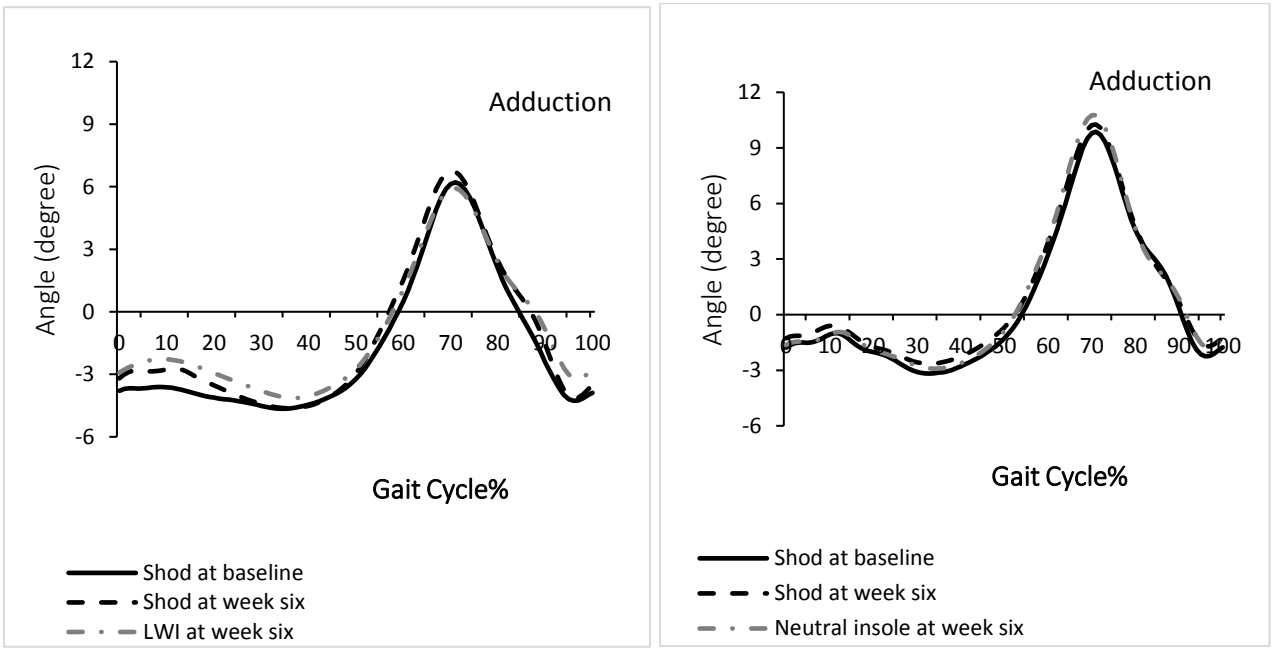

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Figure 4-31: The knee angle in frontal plane for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.9.5. Ankle angle in sagittal plane for the two groups

There was no significant difference between groups ($p \geq 0.05$) and the ANOVA analysis has also showed that there is no significant interaction between groups and weeks ($p \geq 0.05$) on the ankle dorsiflexion angle, the ankle plantar-flexion angle and the ankle ROM in sagittal plane. Whereas, the effect of weeks on ankle dorsiflexion angle, the ankle ROM in sagittal plane was significant ($p < 0.05$). The descriptive data is presented in table 4-40.

After wearing LWI for six weeks, the ankle dorsiflexion angle significantly increased (mean difference 0.97(1.1) degree, p=0.04) in comparison to the shod at baseline. The ankle ROM in sagittal plane slightly increased but not significant (mean difference 1.6(3.3) degree, p=0.09) after wearing LWI for six weeks in comparison to the shod at baseline. In addition, there was no significant change within group, in comparator group, in different time points or compared to LWI group in the ankle dorsiflexion angle, the ankle plantar flexion and sagittal ankle ROM (Figure 4-32).

Table 4-40: Mean (SD) ankle angle in sagittal plane during walking for two groups after wearing insoles for six weeks.

Ankle angle	Mean (SD)					
	Baseline (week 0)		Week Six			
	Wedged Group	Neutral Group	Wedged Group		Neutral Group	
			Shod	LWI	Shod	Neutral insole
Ankle dorsiflexion (degree)	20.16 (3.9)	22.12 (3.3)	21.02 (3.7)	21.13* (3.5)	22.20 (3.6)	22.41 (3.6)
Ankle plantar-flexion (degree)	-6.44 (6.1)	-5.38 (5.0)	-5.81 (5.5)	-7.05 (5.1)	-5.4 (4.5)	-6.44 (4.7)
Ankle ROM (degree)	26.60 (5.3)	27.51 (3.5)	26.83 (4.58)	28.17 (5.0)	27.69 (4.2)	28.8 (4.0)

***** Significant difference compared to baseline ($p<0.05$).

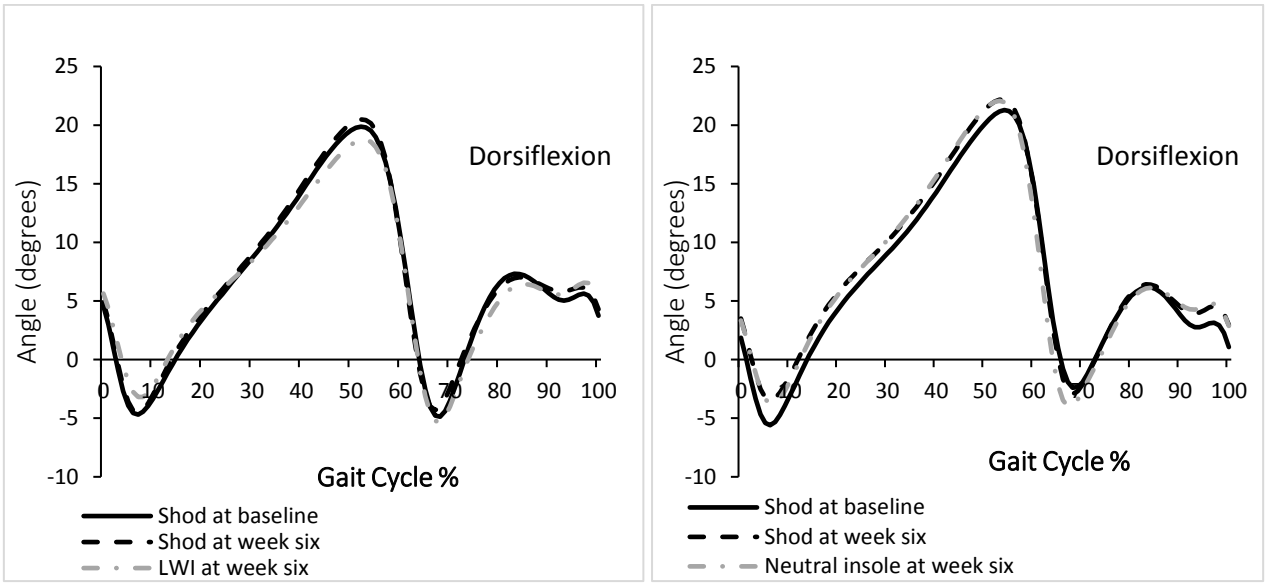

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Figure 4-32: The ankle angle in sagittal plane for (a) intervention group (lateral wedged insoles) and (b) comparator group (neutral insoles) at different time points.

4.10.10. Questionnaire and function tasks results

Symptoms, activity of daily living (ADL), sports & recreational activity, quality of life (QoL) subscales of KOOS questionnaire, intermittent and constant osteoarthritis pain (ICOP) questionnaire, physical activity scale for elderly (PASE), aggregated locomotor function (ALF) addition to short form health survey (SF-12) (physical component scale (PCS) & mental component scale (MCS)) were completed at baseline (pre- intervention) and week-six (post-intervention). The mean, SD, mean difference and p-values for both groups are presented in table 4-41. There was a significant difference between LWLs group and comparator group on KOOS- function in sports & recreational activities and physical component scale of SF-12 health survey. Therefore, these variables were improved when the individuals with medial knee OA wore the wedged insoles for six weeks compare to the comparator group. Knee pain (ICOP) was improved within groups for both insoles with no significant differences in between groups.

After wearing the LWIs for six weeks, there was a significant improvement ($p<0.05$) in KOOS symptoms subscale, function in sports & recreational activities, ICOP, physical component scale of SF-12 health survey, and ALF score in LWI group compared to baseline.

Table 4-41: Mean (SD) and mean differences in questionnaires/function changes within and between groups after wearing insoles for six weeks.

	Mean (SD) LWI		Mean (SD) N		Mean (SD) difference within Group (Week 6 - Week 0)		Mean difference between Groups
	Week 0	Week 6	Week 0	Week 6	LWI	N	LWI vs. N
KOOS							
Symptoms	60.7 (14.1)	70 (18.15)	64.7 (19.9)	68.5 (20.4)	9.3 (12.7) **0.006***	3.8 (3.97) 0.22	-5.5 0.219
ADL	63 (19.6)	71.6 (19.6)	61.1 (14.6)	63.1 (12.4)	8.6 (19.0) 0.114	2.0 (13.2) 0.703	-6.6 0.379
Sports & recreational	39.5 (29.1)	58.2 (34.09)	30 (28.2)	29 (22.1)	18.7 (19.6) **0.004***	1.0 (16.1) 0.862	-19.7 **0.025****
QoL	36.9 (20.29)	46.4 (14.8)	44.6 (16.9)	47.1 (11.9)	9.5 (15.8) 0.06	2.5 (14.0) 0.604	-7.0 0.310
ICOP	47.44 (17.5)	37.03 (16.3)	48.87 (14.33)	39.23 (10.79)	10.4 (10.9) **0.025***	9.6 (15.9) **0.036***	-0.77 0.9
PASE	105.96 (66.83)	133.40 (67.39)	118.75 (92.65)	132.8 (90.48)	27.4 (52.9) 0.108	14.1 (49.5) 0.39	-13.39 0.566
SF-12							
PCS	34.89 (10)	39.94 (9.58)	33.68 (6.96)	30.18 (4.23)	5.05 (5.81) **0.005***	-3.5(3.83) **0.037***	-8.55 **0.001****
MCS	49.81 (9.83)	52.38 (10.24)	48.36 (9.20)	51.83 (6.93)	2.57 (6.68) 0.358	3.47(10.2) 0.219	0.9 0.818
ALF (in second)	19.70 (4.99)	13.50 (1.65)	15.40 (5.25)	15.40 (4.90)	6.20 (5.47) **0.000***	0.0 (2.2) 1	6.2 **0.004****

*significant difference compare baseline

**significant difference between groups (at week 6)

4.10.11. Dynamic balance results

Mean, SD, and differences within and between groups of raw and normalised data of the both groups are presented in table 4-42. After wearing LWIs over six weeks, dynamic balance in individuals with medial knee OA significantly improved in the medial direction compare to baseline and comparator group ($p<0.05$). However, there was improvement in anterior direction for wedged group but not significant compared to baseline, whereas the anterior direction of SEBT improved significantly in LWI group compared to comparator group.

Table 4-42: Mean (SD) and mean differences in dynamic balance changes within and between groups after wearing insoles for six weeks.

Direction	Mean (SD)		Mean (SD)		Mean (SD) difference within Group		Mean difference between Groups
	week 0		week 6		Week 0 vs. Week 6		
	LWI	N	LWI	N	LWI	N	LWI vs. N
Raw Data							
Anterior (cm)	51.66 (13.6)	55.13 (8.98)	56.86 (12.2)	50.93 (11.8)	5.20 (8.50) P=0.061	-4.20 (7.9) P=0.124	9.4 **P=0.02****
Medial (cm)	45.16 (11.3)	51.22 (12.43)	51.36 (12.12)	48.50 (12.2)	6.20 (4.42) **P=0.003****	-2.73 (6.82) P=0.15	8.9 **P=0.003****
Normalised data							
Anterior (%)*	57.06 (15.2)	59.86 (10.7)	62.82 (13.7)	55.2 (12.8)	5.76 (9.23) P=0.056	-4.65 (8.56) P=0.116	10.41 **P=0.017****
Medial (%)	49.87 (12.5)	55.47 (13.5)	56.87 (14.09)	52.51 (12.7)	7.0 (5.28) **P=0.003****	-2.96 (7.61) P=0.16	9.96 **P=0.003****

*percentage of lower limb length
**Significant value P<0.05

4.10.12. Cumulative knee loading (CKL)

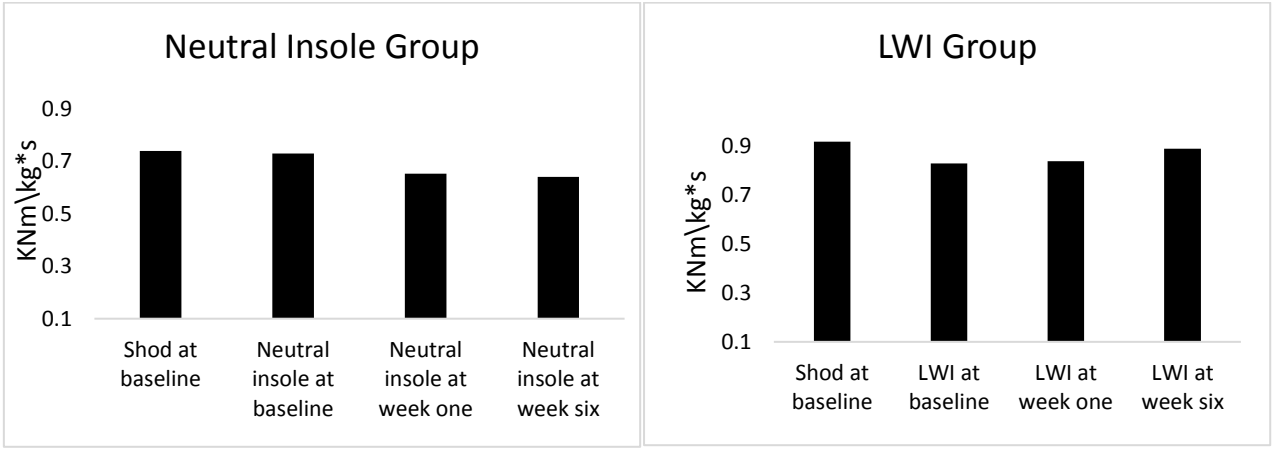
There was no significant difference between groups (p=0.328). The ANOVA analysis has also showed that there is no significant interaction between groups and weeks (p=0.461) on n the CKL. The main effect of weeks was not significant on the CKL (p=0.357). After wearing insoles (either LWI or neutral insole), there were no significant changes in week one and week six compared to baseline and comparator group ($p \geq 0.05$). The descriptive data is presented in table 4-43.

The CKL reduced in LWI group at baseline, week one and week six by 10.2%, 16.9%, and 12.8%, respectively. Whereas the CKL reduced by 1.6%, 5.8%, and 3.6% in baseline, week one, and week six, respectively, in comparator group. The CKL reduced compared to baseline by 8.7% after wearing LWI for one week even though the number of steps increased by 603 whereas, it reduced by 11.7% after wearing neutral insole for one week even though the number of steps reduced by 805 steps/day. The CKL reduced compared to baseline by 3.4% after wearing LWI for six weeks even though the number of steps increased by 1525 steps/day whereas it reduced by 13.3% after wearing neutral insole for six weeks even though the number of steps reduced by 810 steps/day.

Table 4-43: Mean (SD), percentage of changes and p-value in CKL during walking for two groups after wearing insoles for one and six weeks.

	Baseline				Week One				Week Six			
	Wedged Group		Neutral Group		Wedged Group		Neutral Group		Wedged Group		Neutral Group	
	Shod	LWI	Shod	Neutral insole	Shod	LWI	Shod	Neutral insole	Shod	LWI	Shod	Neutral insole
Mean(SD) (KNm\kg*S)	0.92 (0.5)	0.83 (0.5)	0.74 (0.35)	0.73 (0.38)	1.02 (0.5)	0.84 (0.45)	0.69 (0.3)	0.65 (0.35)	1.02 (0.49)	0.89 (0.49)	0.67 (0.39)	0.64 (0.35)
% Change	-10.2%		-1.6%		-16.9%		-5.8%		-12.8%		-3.6%	

Figure 4-33: Cumulative knee loading for two groups at different time points.



4.11. Discussion

The effect of nonsurgical foot and ankle interventions such as lateral wedged insoles (LWI), are highlighted and are recommended in the management of medial knee osteoarthritis (OA) in 13 out of 14 clinical guidelines, based on beneficial findings regarding pain, function, and knee loading reductions. The reduction in the External Knee Adduction Moment (EKAM) with LWI has been found in the majority of the studies, with pain and function improving significantly compared with no intervention (control group). However, these improvements in terms of pain and function do not appear when compared with a comparator insole group (neutral insole). Therefore, there is a conflict in the findings between biomechanical studies and clinical trials which means adoption of the insoles can be challenging as clinicians are more driven by pain reduction rather than mechanical reduction. Therefore, there is a need to investigate whether other factors are creating these non-significant clinical findings. The current study was undertaken to investigate the effect that lateral wedged insole have on EKAM, knee pain, and activity level over one and six weeks where this study is the first study to look into the change in these variables together as a primary outcome after lateral wedged insole intervention. As this study assessed two groups, firstly we evaluated whether there were any differences between these groups at baseline and the general knee osteoarthritis literature.

4.11.1. The characteristics of the participants at baseline compared to the current literature

At the baseline assessment before any intervention, twenty male individuals were recruited in the current study who had been diagnosed with medial knee osteoarthritis; mean age 61.1 (9.4) years (age range 47-78 years), mean height 174.1 (8.5) cm (height range 161-191 cm), mean mass 83 (18.9) kg (mass range 51-119 kg), mean BMI 26.9 (4.8) kg/m^2; BMI range 18.3-34.7 kg/m^2. The mean of EKAM, KAAI, number of daily steps, and knee pain at baseline in this study were 0.41 (0.13) Nm/kg, 2.42 (0.84) %Bw.ht, 0.26 (0.08) (Nm/kg).s, 6673 (3368) steps/day, 50.8 (13.5), respectively.

The EKAM at baseline in the current study is in agreement with Jones et al., (2013b & 2015), Al-Khlaifat et al., (2016) and Al-Zahrani et al., (2016) where EKAMs were 0.38 Nm/kg, 0.39 Nm/kg, 0.34 Nm/kg and 0.44Nm/kg, respectively, all these data were collected in the same gait laboratory. The data in the current study is similar in nature to the previously collected lab data. The EKAMs at baseline were lower in Chang et al., (2015) where the mean EKAM was 1.67 %Bw.ht. One of the potential reasons that the EKAM was lower is that the majority of individuals at baseline (70.3%) in Chang et al (2015) study (70.3%) were diagnosed with mild knee OA (K/L grade ≥ 2) and thereby

EKAM was lower (Foroughi et al., 2009). Whereas, in the current study individuals with mild-moderate medial knee OA (K/L grade 2 or 3) were assessed. In Hinman et al., (2009) study, the EKAM at baseline was higher (3.82 %Bw.ht) compared to the current study, this may be because the magnitude of mean walking speed at baseline was higher in the Hinman et al (2009) study (1.27 m/s).

As expected, the Knee Adduction Angular Impulse (KAAI) at baseline in the current study is in agreement with of Jones et al., (2013b), Keen et al., (2015), Jones et al., (2015), Al-Khlaifat et al., (2016), and Al-Zahrani et al., (2016) where KAAIs were 0.15 (Nm/kg).s, 0.19 (Nm/kg).s, 0.16 (Nm/kg).s, 0.12 (Nm/kg).s, 0.14 (Nm/kg).s, respectively.

The average of number of steps, at the baseline assessment in the current study, is in agreement with a large observational study performed by White et al., (2015) where the mean number of steps was 6650 steps/day (±2741). In Bennell et al., (2011), the participants in both groups stepped further with 7735 steps/day (±3652) at the baseline. Moreover, a recent review of normative data reported that individuals with chronic disease that may limit mobility stepped between 1200 and 8800 steps/day (Tuder-Locke et al., 2009). Hurley et al., (2015) found that individuals with knee OA walked an average of 6518 steps/day which is in agreement with the current study. From a clinical perspective, the pain scale of the KOOS is slightly above the results in Al-Khlaifat et al., (2016), and Al-Zahrani et al., (2016) studies where pain in individuals with medial knee OA at baseline were 34,5 and 33.18, respectively. Whereas in Kumer et al (2013) KOOS pain was high (64.2) in individuals with medial knee OA compare to healthy subjects. This may be because the individuals with medial knee OA in Kumer et al., (2913) study had a higher EKAM at the first peak compared with healthy individuals.

Therefore, the baseline results of EKAM, KAAI, number of daily steps, and Knee Injury and Osteoarthritis Outcome Score (KOOS) pain subscale (primary outcomes) of this study are in agreement with the majority of the current literature. This allows us to set the results in context of this literature and be able to broaden the knowledge base in this area.

4.11.2. Summary of the results

The present study was undertaken to investigate the effect of lateral wedged insoles (LWI) on the EKAM, knee pain, and physical activity level in individuals with medial knee OA. The individuals were assessed in two different time points; one week after baseline assessment and six weeks after baseline assessment. There were no significantly differences between groups at baseline were found in participant demographic, EKAM, pain score, and level of activity. This allows the comparison between groups to be undertaken and the following will summarise the results, both at the different time points and between groups.

<u>After one week of wearing insoles</u>

After one week, the first peak of the EKAM was significantly reduced in the LWI group compared to the baseline and the comparator insole group whereas, the second peak of the EKAM significantly reduced in the LWI group compared to baseline but there was no significant difference between groups. The knee adduction angular impulse (KAAI) was reduced significantly in the LWI group only compared to baseline with no significant differences seen between groups. Over one week, knee pain significantly improved in both groups compared to the baseline but there was no significant difference between groups after using insoles.

There was no significant change within group and between-groups in terms of ground reaction force (GRF), cumulative knee loading (CKL), knee moment in sagittal plane, hip angle in sagittal plane, knee angle in sagittal plane, knee angle in frontal plane, ankle angle in sagittal plane. Whereas, range of motion (ROM) of the sagittal plane ankle angle was significantly increased in LWI group compared to baseline.

The temporal and spatial variables were improved in both groups after one week compared to baseline except stance time and cadence not improving in comparator group compared to baseline. Cadence was significantly increased in LWI group over one week compared with the comparator group. While, walking speed increased in LWI group compared with the comparator group but not significant.

<u>After six week of wearing insole</u>

After six weeks, the first peak of the EKAM was significantly reduced in the LWI group compared to the baseline and comparator group whereas, the second peak of the EKAM was significantly reduced in the LWI group compared to baseline but not between groups. Only in the LWI group was KAAI significantly reduced compared to the baseline and the comparator group after six weeks of using the LWI.

After six weeks, there were no significant differences between-groups in terms of symptoms subscale, Activity of Daily Living (ADL) subscale, and Quality of Life (QoL) subscale over six weeks. Whereas, there was a significant improvement in LWI group compared to the comparator group over the six weeks in the sport & recreational subscale. However, when compared to baseline, the LWI group did show a significant reduction in symptoms and the sport & recreational subscales.

There was a significant improvement in the LWI group compared to the comparator group over the six weeks in terms of Aggregated Locomotor Function score (ALF), and anterior & medial directions of Star Excursion Balance Test (SEBT). ALF and the medial direction of SEBT were also significantly improved in the LWI group compared to baseline.

After six weeks, Intermittent and Constant Osteoarthritis Pain (ICOP) and Physical Component Scale (PCS) of 12-Items Short-Form Health Survey (SF-12) were improved significantly in both groups compared to baselines. Whereas, PCS of SF-12 significantly improved only in the LWI group compared to the comparator group

There were no significant changes within group or between-groups in terms of GRF, CKL, knee extension moment, hip angle in sagittal plane, knee angle in sagittal plane, knee angle in frontal plane, ankle angle in sagittal plane. Whereas, knee flexion moment, ROM of knee in sagittal plane and ankle dorsi-flexion angle were significantly increased in LWI group compared to the baseline.

The temporal and spatial variables were significantly increased in the LWI group over the six weeks compared to the baseline, except the unaffected step length did not change significantly. Speed, stride length, cadence and affected and unaffected step length were increased in comparator group compared to baseline whereas, affected and unaffected stance time did not change significantly. There was no significant change between groups after six weeks.

The results achieved in the study will now be contemporised in terms of where these fit with the current literature focussing on the specific hypotheses stated earlier in the thesis.

4.11.3. The comparison of the two insoles on the EKAM

Null hypothesis 1, There will be no significant reduction in the external knee adduction moment in the group using the lateral wedged insole compared to the comparator group.

The null hypothesis was rejected as the LWI group reduced the first peak of the EKAM at both one and six weeks compared to the comparator group and also compared to the baseline. However, participants in weeks one and six demonstrated faster walking speed in LWI group compared to baseline and this could increase loads at the knee joint, the EKAM significantly reduced after wearing LWI due to the effect of the LWI on the knee joint. LWI are designed to reduce the loading on the medial compartment of knee joint by alter the position of the centre of pressure under the foot and thereby displace the GRF laterally with respect to the knee joint (Yasuda and Sasaki, 1987; Hinman et al., 2013). One of the primary mechanisms in the external knee adduction moment is the vertical GRF. The vertical GRF did not change significantly between groups and visits although, the vertical ground reaction forces increased by 3% and 4% after wearing the LWI for one and six weeks, respectively, compared to the baseline. This is explained by the strong correlation between high ground reaction forces and faster acceleration (Winter, 1984; Shelburne et al., 2006) where walking speeds increased in LWI group, so one would expect that the EKAM have a corresponding increase, which was not found. With no significant change in vertical ground reaction forces in the LWI group, the EKAM would have been reduced by another mechanism. This mechanism is determined the reduction in the length (distance) of the moment arm when wearing the LWI. The LWI acts to displace the line of the GRF more laterally to the centre of the knee joint by altering the calcaneus (rearfoot) into valgus position (Pollo, 1998). The maximum effect of the LWI happens during the early stance period of stance phase (first peak of the EKAM) because of the structure of the LWI where the inclination of the insole was greater (5˚) at the heel and gradually decreased to 0˚ at the 5th metatarsal head. The first peak of the EKAM significantly reduced after wearing the LWI for one and six weeks by 15% and 16.8%, respectively, compared to the baseline. Therefore, the knee load reduced and disease progression may be delayed (Miyazaki et al., 2002).

Whereas, the second peak of the EKAM significantly reduced after wearing LWI for one and six weeks by 14.2% and 10%, respectively, compared to the baseline. The wedged gradually decreases under the mid and forefoot, therefore the 0˚ of inclination of the LWI at the 5th metatarsal head may be the reason of no significant difference between groups was found in term of the second peak of the EKAM (late stance peak).

The KAAI was reduced significantly after wearing LWI at both one and six weeks compared to the baseline but no change was recorded in comparator group compared to baseline. After wearing LWI for six weeks, there was a significant reduction in the KAAI compared to comparator group. The results of the current study are in the agreement with the majority of the studies (Kerrigan et al., 2002; Hinman et al., 2008, 2009 & 2012; Barrios et al., 2013; Jones et al., 2013a, 2013b, 2014 & 2015). In the current study, the EKAM and KAAI reduced by 12% and 11.6%, 15% and 17.8%, and 16.8% and 22% after immediately, one week, six weeks, respectively, of wearing LWI compared to baseline. These results of the current study are in agreement with a crossover randomized study (Jones et al., 2013a) where the EKAM and KAAI reduced by 12% and 7%, respectively, after wearing LWI for two weeks compared to baseline.

Hinman et al., (2012) found that the EKAM and KAAI significantly reduced by 5.8% and 6.3% as an immediately effect of wearing LWI. The participants in Hinman et al., (2012) study wore LWI without a medial support whereas LWI with medial support were worn in the current study. Kerrigan et al (2002) investigated the immediately effect of LWI without support and they found that the EKAM significantly reduced by 6% compared to the baseline (no insole). The reduction in the EKAM was diminished when using LWI without medial support and the difference was 1.08% for LWI with medial support; however, there was no significant difference between to kind of insole in term of EKAM reduction (Jones et al., 2014). Therefore, the structure of the LWI, for example that used in Hinman et al., (2012) study, may be the reason of that lower reduction in the EKAM in Hinman et al., (2012) study compared to the current study. In addition, the material of the LWI particularly the densities of the insole may be the reason of variability in the EKAM reduction. Hinman et al., (2012) tested LWI with a durometer score 57.5 and Kerrigan et al., (2002) used LWI with durometer score of 55, while the density of the LWI in the current study was 70 which stiffer insoles were recommended (Radzimski et al., 2012) and used (Jones et al., 2014) to treat medial knee OA.

In addition, a significant reduction in the EKAM was found when the immediate effect of LWI has been investigated compared participant's shoes in forty participants with medial knee OA (Hinman et al., 2008) which is slightly lower compared with the current study. The majority of the participants demonstrated a reduction in the first peak of the EKAM from 0.1% - 18.2% (Hinman et al., 2008) and 1.9%-27% in the current study. One of the potential reason the reduction of the first peak of the EKAM was greater is that a high density LWI (70) were worn bilaterally inside the participants's own shoes in the current study which has an efficient effect compared to the medium density (57.5) that worn inside control shoes in Hinman et al., (2008). In addition, it is recommended that

participant's own shoes be used as control conditions to ensure they do no experience a large biomechanical change (Lewinson et al., 2016)

The results of the current study support Jones et al., (2013b) study who found as similar effect of LWI in 28 participants with medial knee OA. They found that the EKAM and KAAI reduced significantly by 10%, 14.2%, and 10% and 7.14% when wearing LWI with and without medial support, respectively, compared to control shod. Possible explanation for the reported greater reduction in the EKAM at early stance phase in the current study might be due to the participants in the current study wore their shoes as control insole and LWIs were inserted in their own shoes. Therefore, the nature of the shoes of the participants may play a role biomechanical changing (Lewinson et al., 2016). However, the same shoe that worn at baseline for each participant was worn at both visits. Other potential reason is that the LWI in the current study was designed with medial support to achieve a maximum effect regarding the studies (Jones et al., 2014).

The results of the current study are in agreement with one month results reported by Hinman et al., (2009) and one year results reported by Barrios et al., (2013). However, Hinman et al., (2009) observed lower EKAM reduction (between 4.2% and 7.4%) at both baseline and after one month, this may be because they used low density (57.5 shore) compared to the current study. Barrios et al., (2013) found the percentage of EKAM reduction after wearing LWI for one year was maintained at 8% as baseline result. In the current study, the EKAM reduction at baseline, week one and week six in the LWI group appeared to remain consistent or increased throughout the six weeks of intervention where reductions were 12%, 15% and 16.8%, respectively. The possible reason for reported grater reduction EKAM and KAAI in the current study might be due to the LWIs which used in the current study were with medial support that designs to offer greater reduction in the knee loading in healthy subjects by provide a better function foot by reduction ankle complex eversion angle (Jones et al., 2014). In addition, comfort score was not measured in Hinman et al., (2009) and Barrios et al., (2013) who used LWI without supported arch and thereby we assume the LWI without medial support may diminish the biomechanical effectiveness of LWI. The LWIs were found to be comfortable with the majority of the participants (75%) with high adherence (wearing time, average, 6.5-7.5 hours/day) in the current study. However, Hinman et al., (2009) concluded that the reduction of the EKAM did not decease over the time which is this result support by the current study. Moreover, the LWI with 70 shore density and medial support was used in the current study which offer greater reduction on the EKAM.

Putting the reduction in first peak of EKAM into context, a large cohort study found that both peak EKAM and KAAI were associated with joint narrowing and cartilage loss over 12 months (Bennell et al., 2011a), 24 months (Chang et al., 2015) of follow-up and the risk of progression of knee OA increased 6.46 times when the EKAM increases by 1% on the 1st peak (Miyazaki et al., 2002). Therefore, reduced the EKAM in the current study by more than 12% when wearing LWI could delay the progression of knee OA.

4.11.4. The effect of the lateral wedged insole on the level of the activity

Null hypothesis 2, There will be no significant difference in level of physical activity in the group using the lateral wedged insole compared to the comparator group.

In the present study, the effectiveness of the LWIs on the level of physical activity in individuals with medial knee OA was investigated after wearing the insoles. The null hypothesis was partially rejected as the changes in the time spent in stepping between week one and baseline between the LWI group and comparator group increased significantly. In week six of wearing the insoles, the changes between week six and baseline in both the number of steps and the stepping time increased significantly in LWI group compared to the comparator group. Whereas, there were no significant differences in the rest of level of activity variables between-groups at both time points. There was no significant differences between groups when measured by the PASE self-reported questionnaire as the PASE cannot determine changes in physical activity between time-points.

The current results of level of physical activity show that the number of steps and stepping time significantly increased by 1,525 steps/day and 17 min/day, respectively, in week six compared to baseline in the LWI group, but this was not seen in week one or in the comparator group. One of the potential reason there was no significant change in week one compared to baseline in the LWI group could be that the effect of LWI on level of activity takes longer to have an effect on the individuals. The other potential reason is that the individuals may change their typical inactive physical behaviour realise that they do more walking based activities. This would be seen as a positive influence of the insoles especially from a public health perspective as the individuals are doing more which would improve their general level of social interaction and also wellbeing. Regarding the other variables of physical activity such as sedentary time, standing time, up-right time, small changes were seen when individuals wore LWI but not significant. These changes may have become more pronounced if the sample size was larger or a longer intervention period was undertaken but

promising results nevertheless are seen in these measures. Therefore, in the current study, the participants in the group wearing LWIs demonstrated a change in activity profiles after six weeks.

In this research and previous research, the actual number of steps is usually only presented, however, the cadence band at which the individual is walking is a vital aspect of this. This would demonstrate more purposeful walking and increases in the cadence bands (90-100 and 100-110 steps/min) would highlight these changes. The LWI group showed an increase in number of steps taken at a cadence above 90 steps/minute and in continuous stepping bouts of greater than 5 minutes. This was not seen in the comparator group. From thesis results, it can be seen that the pattern of walking improved when the participants were wearing LWI where they walked 5-10 minutes continuously for longer duration in the day in both week-one and week-six compared to baseline which infers that total walking length is increased. In addition, the amount of time walking per day at cadence 90-100 steps/day and 100-110 steps/days increased which demonstrated that they had a faster and more purposeful walking. The step length was not measured and while individuals in the current study increased their cadence and speed but they could have taken smaller and more steps.

Therefore, Individuals walked more, walked faster and for a longer duration when wearing LWI whereas no change was seen in comparator group. Surprisingly, the current study showed that changing the activity behaviour of individuals of knee OA was not complex with using LWI because LWI is an inexpensive, easy to use and there is no need to follow a long or complicated treatment programme to change the activity behaviour as in behaviour modification programmes with obese subjects (Bravata et al., 2007). However, the long-term change in an individual's activity after a longer period of intervention is needed to determine whether these changes at six weeks are maintained. If this is the case, then the role of lateral wedge insoles in the treatment of medial knee osteoarthritis is linked with changes in the wellbeing of the individual.

The present study is the first study that has investigated the effectiveness of LWI on level of activity (volume and pattern); however, the number of steps was measured after wearing LWI in a previous study (Bennell et al., 2011b). In this study, they measured the number of steps at baseline and after wearing LWI for 12 months. In this study, they did not find any differences between these time-points and groups and been because the number of steps increased at different time-points between baseline and one year and authors missed to measure it, but only have a pre-post 12-month assessment. The non-significant change in the number of steps may also have been due to the knee pain or the individuals comfort with the insole. In the study, a large proportion of the LWI users found them uncomfortable (47%) (Bennell et al., 2011b). This would have meant that the individuals

did not change their profile and also is a potential reason for the non-significant pain reduction as adherence was low. However, in the current study, a large proportion of the individuals in LWI group found LWI comfortable (75%) with high adherence. Recent evidence has found that comfort score and pain rate were strongly correlated in individuals with medial knee OA (Jones et al., 2014).

Individuals with medial knee osteoarthritis have problems with sustained standing due to excessive knee pain. Prolonged standing with abnormal knee loading in individuals with knee OA may lead to detrimental stress on affected knee joint and exacerbates knee pain (McAlindon et al., 1992; Sun, 2010). The change in the time spent in different postures after wearing LWI was measured in the current study to determine any change in time spent in standing (weight-bearing activity) or sedentary time. When using the LWI in the current study, a small change in standing time, but not significant was found and there was a decrease sedentary time. Sedentary behaviour (inactive) in individuals with knee OA (Dunlop et al., 2011) increases the risk of serious diseases such as obesity, diabetes and cardiovascular disease (Pederson et al., 2006). Therefore, by reducing sedentary behaviour by the LWI reduces cardiovascular disease, weight gain (Pedersen et al., 2006; Dumurgir et al., 2009), and improved muscles power (Bravata et al., 2007).

In addition, reducing sedentary behaviour time is important for cartilage structure because low levels of activity have been associated with greater progression of cartilage loss (Stehling et al., 2011; Lin et al., 2013). Evidence was found that when there was the absence of normal joint loading in the knee in patients with spinal cord injury, this led to cartilage atrophy (Vanwanseele et al., 2002). In the current study the number of steps increased from a lower physical activity bands (6,415 steps/day) at baseline to a somewhat or moderate level of activity (7,940 steps/day) after wearing LWI for six weeks. These classifications of physical activity bands is according to the daily number of steps (Tudor-Locke and Bassett, 2004) and recommended by a recent review that performed by Gate et al (2015). If you contextualise these recommendations with the current findings, these improvements are deemed to be beneficial for the physical health and wellbeing of the individual.

In addition, in the current, physical activity in LWI group when measured with PASE (106) is considered as lower physical activity and the PASE improved to a moderate physical activity (133.4) after six week of wearing LWI compared to baseline. The PASE improved from 118.8 to 132.8 after six week of wearing neutral insole compared to baseline with no significant differences was seen between groups. An interesting point can be noticed from these results is that the PASE cannot detect changes in physical activity within-group, even there was improvement. Those classification of physical activity is according to amount, scoring, of ability to do light, moderate, and vigorous

activities such as occupational, household, and leisure activities (Lin et al., 2013). Therefore, improving the level of physical activity in individuals with knee OA has been recommended by the majority of the studies (White et al., 2013 & 2014; Lin et al., 2013; Gate et al., 2017) and it has been achieved by wearing LWI in the present study. Whether these improvements persist after longer durations needs to be evaluated but the initial signs are positive.

4.11.5. The effect of the lateral wedged insole on pain and function.

Null hypothesis 3a, There will be no significant difference in knee pain in the group using the lateral wedged insole compared to the comparator group.

Null hypothesis 3b, There will be no significant difference in function the group using the lateral wedged insole compared to the comparator group.

When prescribing an intervention for an individual with medial knee osteoarthritis, the primary reason for this would be to reduce the pain the individual is suffering from. Secondly, if a reduction in pain was seen, one would hope to see an increase in physical function. Therefore, understanding the changes seen both between insoles and between time-points is important. When looking at the KOOS pain subscale, this significantly improved within group for each group (LWI & neutral insoles) compared to baseline, but there were no significant differences between-group at week one. In addition, at week six compared to baseline, KOOS pain subscale and ICOP significantly improved within group for each group (LWI & neutral insole) compared to baseline, but there were no significant differences between-group at week six. Therefore, the null hypothesis was accepted in term of knee pain as there was no significant difference between LWI group and comparator group. All KOOS subscales did not improve after wearing either LWI for six weeks compared to comparator group while KOOS sport & recreational subscale improved in LWI group compared to comparator group, where no changes were seen in comparator group compared to baseline. KOOS symptoms and sport & recreational subscales were improved after wearing LWI for six weeks compared to baseline. The physical function when measuring by ALF was improved significantly after wearing LWI for six weeks compared to baseline and comparator group, where no change was seen in comparator group. Therefore, the null hypothesis in term of function was partially rejected as there was a significant improvement in ALF compared to comparator insole.

In this study, improvements in knee pain were seen at week one and week six in the LWI group and comparator group compared baseline which was accompanied with the reduction in the EKAM with LWI insoles. We assume these results indicate that the altered EKAM from the LWI enabled pain

and function to improve. Therefore, participants who have a reduction in the EKAM may they experienced reduction in knee pain which leads to increased levels of activity, and whereby the individuals would walk to their respective pain level, in other words the pain level which stops them from functioning as at baseline. In the current study, the EKAM reduction, pain and function improvement, and improvement in physical activity have been noticed in the LWI group. This reduced pain has increased the number of steps significantly in the LWI group in week six compared to the baseline and comparator group with roughly consistent pain reduction, whereby pain improved by 28% and 25% in week one and week six, respectively. This may be explained by the total number of steps may increase in the absence of knee pain (Wideman et al., 2014; White et al., 2014) result in the EKAM reduction by wearing LWI.

Conversely, however, knee pain improved significantly in the comparator group in week one and week six compared to baseline, but the total number of steps was decreased by approximately 800 steps/day. Knee pain was measured subjectively (self-reported questionnaires) which have been found to be influenced by human memory, which may be weak in older individuals, and an inability to answer accurately or completely (Maly et al., 2006). Therefore, this reduction in physical activity (total steps) in the comparator group may be due to greater knee loading and the individuals may experience knee pain during movement and the improvement in knee pain (in pain scales) with comparator group was placebo. In addition, in comparator group, knee pain improved in week one and week six by 36% and 23%, respectively, when measured by KOOS pain subscale. This improvement in knee pain was noticed in individuals with neutral insole because they may potentially receive a placebo effect from the neutral insole (Parkes et al., 2013) where a change in a person's symptoms (i.e. knee pain) as a result of getting placebo is called the placebo effect and due to person's expectations (Hróbjartsson & Gotzsche, 2004). However, the EKAM did not change significantly in week one and week six compared to baseline in this group. In addition, this change in knee pain did not reflect on the physical activity in this group. Evidence suggests that the therapeutic benefits associated with placebo effects do not alter biomechanical changes in individuals with medial knee OA (Jones et al., 2014).

Knee pain and function improvement were found when using LWI in comparison with baseline in individuals with medial knee OA (Hinman et al., 2008; Barrios et al., 2009b & 2013; Jones et al., 2013a; Hatef et al., 2014). Knee pain reduced by 28% and 25% in LWI group at week one and week six, respectively, compared to baseline and these results agree with Hinman et al., (2008) where they found that knee pain reduced by 22% after 3 months of wearing LWI compared to baseline (participant's shoes). In addition, the mean reductions of the 1st peak of the EKAM were 5-9% and

15-16.8% in Hinman et al (2008) study and the current study, respectively. Hinman et al., (2008) found that the physical function improved significantly (measured by WOMAC) after 3 months of wearing LWI compared to baseline (participant's shoes). Moreover, the physical function was improved significantly in LWI group where in neutral insole did not compared to the baseline (Hatef et al., 2014).

The current results are in agreement with a prospective study by Barrios et al., (2009b) where sixty-six patients were divided in two groups; LWI group and neutral insole group for one year. Significant reduction in knee pain (WOMAC) and function improvement (in both groups was found at one month and one-year follow-up compared to baseline with no significant change was seen between groups (Barrios et al.,2009b). The current results are in agreement with Hatef et al., (2014) where the participants were randomised to either a 5˚ lateral wedged insole or neutral insole for two months; the mean differences were 29.3% and 6.25% for LWI and neutral insole, respectively, compared to baseline (within group) with a significant pain improvement in both groups. The potential reason the knee pain reduced in LWI group is that the knee loading decreased when wearing LWI for two months. However, the EKAM was not measured in their study. The current results are in agreement with a cross-over study by Jones et al., (2013a) where they noticed a significant pain relief and function improvement in individuals with medial knee OA when wearing LWI for 2 weeks compared to baseline (standardised shoe). This suggests that pain relief and the function improvement reported by individuals with medial knee OA when wearing LWIs are probably due to unloading of the medial knee compartment which enabling pain and function to become better.

The current results are in contrast to the results of Baker et al., (2007) and Bennell et al., (2011b). In a cross-over study was performed by Baker et al., (2007), no significant improvement in knee pain and function after wearing LWI for six weeks compared to baseline and neutral insole group. In the Baker et al., (2007) study, the EKAM was not measured therefore, it is no known whether that LWIs which used in their study had a biomechanical effect and knee loading reduced by wearing LWI as density of the LWI was 48 durometer. In addition, although, comfort of wearing insoles and pain ratings were strongly correlated (Jones et al., 2014), comfort score was not measured in Baker et al., (2007) study. The effectiveness of insole on pain may be diminished when use insole with low density. Therefore, we assume LWI caused greater discomfort for participants and therefore, pain response may be affected by the comfort of the insole (Jones et al., 2014). In addition, Bennell et al., (2011b) found that there was no change in pain and function after using LWI for 12-month and no significant differences were seen compared with neutral insole. One of the potential reasons the

pain and function did not change is that the EKAM was no measured in their study and therefore, not known whether LWI had biomechanical effects that are supposed to reflect on the clinical findings. In addition, Bennell and her colleagues (2011b) used a different insoles compared to the current study as a 5˚ LWIs with 57.5 durometer were used which were accompanied with back and foot pain. In the current, the insoles were made of high density (70 durometer) and comfort which offer greater reduction on the EKAM are recommended to treat medial knee OA (Radzimski et al., 2012; Jones et al., 2014 & 2015) and thereby pain improvement was noticed in intervention group compared to baseline due to effectiveness of LWI on pain. The third potential reason is that the knee pain and function were assessed at two time-points (at baseline and after 12 months) with a long gap between them and therefore, some data may be missed.

The improvement in sport and recreational subscale in LWI group may be explained by the effect of LWI occurred by reducing the EKAM and thereby knee pain improved which reflected on the sport activity such as running or jumping. Sport recreation subscale did not improve significantly in comparator group compared to baseline although knee pain improved. In addition, there was no significant change or improvement in activity after wearing neutral insole for one or six weeks compared to baseline using monitor. It is may be because the individuals would receive a placebo effect from comparator group and this placebo improvement in pain did not encourage individuals to change their high level of activity measured by KOOS sport recreation subscale. Same explanation would be applied for ALF when there was no significant change at week six in comparator group compared to baseline in ALF. However, ALF improved significantly at week six in LWI group compared to baseline and comparator group. It may be because the EKAM and pain improved in LWI group and this improvement could be enable function to improve in LWI group. ALF consist of walking eight meters, ascending and descending seven stairs, and transferring from a sitting to standing and because knee pain during movement, such as 6-minute walk task, was a strongly correlated with clinical outcomes in individuals with knee OA (Pakel et al., 2012). Therefore, any improvement in knee pain could be associated with improve in physical function in individuals with knee OA. This explanation is demonstrated in the current study where physical function measured by ALF was improved significantly in LWI group only compared to baseline and comparator group. However, knee pain improved significantly in both groups with no significant difference between groups.

4.11.6. The effect of the lateral wedged insole on the cumulative knee loading.

Null hypothesis 4, There will be no significant difference in cumulative knee loading in the group using the lateral wedged insole compared to the comparator group.

With the reduced EKAM already discussed and the increase in activity level in the group wearing the LWI, it was important to determine whether this would have a deleterious effect on the knee joint in term of cumulative loading (CKL). After wearing LWI for one or six weeks, the CKL did not change significantly compared to baseline and comparator group. The null hypothesis was accepted as there was no significant change in cumulative knee loading after wearing LWI for six weeks compared to baseline and comparator group. To our knowledge, the current study is the first study that has assessed the CKL after wearing LWI. The CKL has been shown to be a highly repeatable measure of daily repetitive and excessive loading on the tibiofemoral joint during free live activity (Robbins et al., 2009). The KAAI with number of steps per day are considered to measure the CKL which can detect any change in knee loading in an environment (Robbins et al., 2009). The CKL is nearly two times greater in individuals with knee OA (Maly et al., 2013) who take fewer steps (white et al., 2014) and walk slower (Dunlop et al., 2011). Therefore, measuring of the CKL was an important in the current study which did not change after wearing LWI for one and six weeks compared to baseline and comparator group. Although, the individuals stepped more when wearing LWI, the CKL did not change significantly compared to baseline. This may be explained by the KAAI reduction when wearing LWI. We assume greater CKL may lead to knee OA or increase disease progression under low daily activity level. In addition, the cumulative loading did not change with improvement in physical activity where knee loading reduced significantly due to the LWI. Therefore, we assume, maintain or reduce the CKL combined with high level of activity may delay progression of knee OA.

A reduction in the EKAM after wearing LWI for six weeks led to a significant increase in the number of steps. PASE scores from 124-242 are considered moderate level of physical activity as Lin et al.,'s (2013) classification. However, there was a reduction in the EKAM whilst wearing LWI at both one and six weeks which led to an improvement in the other variables of physical activity but this was not statistically significant. In addition, an increase in number of steps taken at a cadence above 90 steps/minute and in continuous stepping bouts of greater than 5 minutes were accompanied by a reduction in the EKAM, this improvement in level of activity was not seen in the control group where the EKAM did not change. Therefore, participants walked more, faster and for in long walking bouts when the EKAM reduced. As there is no study has investigated the level of activity

alongside the EKAM at one study, no previous results are available to compare with the current study.

In the current study, number of steps increased by 603 steps/day whilst the EKAM reduced by 15% after wearing LWI for one week compared baseline. In addition, number of steps increased by 1,525 steps/day in week six when the EKAM reduced by 16.8% compared to baseline. Participants spent more time in stepping by 8-17 min/day compared to baseline when the EKAM reduced. For these results, the improvement in level of activity was accompanied by reduction in the EKAM and this improvement was increased by time. This may be explained by the loading on knee joint was reduced by using LWI and pain improvement due to EKAM reduction. The improvement in level of activity was not seen in comparator group when EKAM did not change and there was improvement in knee pain. Therefore, one would expect that this demonstrate that pain only should not be assessed in trials with interventions but also biomechanical parameters and also activity parameters. This also demonstrates that pain cannot be the only outcome when assessing whether interventions are actually effective.

From the current results, it can be noticed that due to the function of the LWI when the line of GRF shifted more laterally to the centre of the knee joint, the EKAM reduced and thereby the level of activity increased in LWI group.

Reduction of the EKAM and reduced pain with increased activity with LWI may be beneficial to the knee joint by delaying disease progression (Miyazaki et al., 2002; Lin et al., 2013). However, there are no long-terms studies assessing the change in progression of knee osteoarthritis which all of these measures over a year. To the best of our knowledge, this is the first study that has assessed level of activity and knee loading in individuals with medial knee OA pre and post-intervention.

When looking at the number of steps, these increased after wearing LWI between 603-1525 steps/day from baseline. Previous studies have found that a high level of activity of stepping more than 10,000 steps/day (Dore et al., 2013) or PASE scores between 242-368 (Lin et al., 2013) was associated with accelerated disease progression likely due to excessive biomechanical load on knee joint. Therefore, from the current results, we can postulate that excessive loading on the knee joint when increasing the number of steps may be diminished when wearing the LWI. However, the participants in the current study did not step more than > 10,000 or scored higher than > 242 on PASE score. Therefore, the risk associated with the increased activity in this group would be reduced on both accounts.

In summary, the study was undertaken to investigate the effectiveness of a LWI on knee loading. The EKAM and KAAI were reduced significantly whereas, the CKL did not change after wearing LWI for one and six weeks even the level of activity was increased. This therefore demonstrates that with an increased activity behaviour knee loading was not generally increased in the LWI group. This is a positive both for future progression studies but also for general physical health.

4.11.7. The effect of lateral wedged insole on the dynamic balance.

Null hypothesis 5, there will be no significant difference in dynamic balance in in the group using the lateral wedged insole compared to the comparator group.

The anterior and medial directions have been measured in this study because these directions are performed by quadriceps and gluteus medius muscles which affected and become weak in individuals with knee OA (Chang et al., 2005). The null hypothesis was rejected as wearing LWI for six weeks improved dynamic balance significantly in anterior and medial directions using modified SEBT compared to comparator group. Dynamic balance in medial direction was significantly improved after wearing LWI for six weeks compared to baseline and comparator group. Dynamic balance in anterior direction was improved after wearing LWI for six weeks compared to baseline but not significant. This could be because the sample size was low in the current study to identify a significant change in the anterior direction of SEBT. However, mean differences in dynamic balance after wearing LWI for six weeks in anterior direction (5.2 cm) and medial direction (6.2 cm) that consider high and clinically significant depends on the values of MDD in chapter three (section 3.5.3). There is no research has investigated the effect of LWI on dynamic balance in knee OA using SEBT except one study that investigated the effect of exercise (Al-Khlaifat et al., 2016). They assessed the dynamic balance in individuals with medial knee OA using SEBT after six weeks of exercises. They found that the affected knee demonstrated significant improvement in the dynamic balance in anterior (A) and medial (M) directions. The mean differences between pre- and post- exercise in A and M directions were 4.50 cm and 5.81 cm, respectively (Al-Khlaifat et al., 2016). Their results are in agreement with the current thesis. The specific causes of balance impairment in individuals with knee OA is still unclear; however, there are various components that effect on balance control such as muscle weakness, aging process, knee pain (accompanied with muscle weakness), and proprioception impairments (Hassan et al., 2001; Lin et al., 2009). In the current study, dynamic balance improved in individuals with medial knee OA after wearing LWI for six weeks. This could be explained by the knee pain reduced in LWI group and thereby

individuals would applied more load on the affected knee to keep their body stable during the test. In addition, individuals may be able to bend their affected knee (support leg) with less pain when preformed the test in LWI group. Therefore, they gained more distance on the SEBT and dynamic balance improved. Our explanation is in agreement with Hassan et al., (2001) who found that higher knee pain with muscle weakness are associated with balance impairment in individuals with knee OA. No study has investigated the effect on the LWI on dynamic balance using modified SEBT and thereby, the current study is the first study that used SEBT after LWI. The SEBT is a reliable to measure dynamic balance in healthy subjects (Kinzey and Armstrong, 1998; Hertel et al., 2000), healthy athletes (Munro and Herrington, 2010), in patients with musculoskeletal conditions such as chronic ankle instability (Hertel et al., 2006), anterior cruciate ligament tears (Herrington et al., 2009), and in individuals with knee OA (chapter three). Therefore, from the results of the current study, LWI could be offer more stability for the individuals with knee OA during activity and improve dynamic balance. However, a future study is needed to determine whether dynamic balance measured with modified SEBT is improved in individuals with knee OA after combined treatment such as LWI with exercise. .

4.11.8. QoL and the EKAM

The SF-12 self-reported questionnaire divides into a physical component scale (PCS) and a mental component scale (MCS). After wearing LWI insoles for six weeks, the PCS improved significantly compared to baseline and comparator group. This improvement in PCS was not noticed after six weeks of wearing neutral insoles compared to baseline. However, Hrobjartsson and Gotzsche (2004) stated that the improvement in self-reported questionnaires may be a placebo effect and could be due to the patient's expectation. A placebo effect was not found in the comparator group and improvement in LWI group may be a result of the EKAM reduction which translated to decreased knee pain and improved level of physical activity (PCS). Whereas, the MCS did not change after six weeks at either LWI group or comparator group compared to baseline or other group. One of the potential reasons is the MCS did not change is that the participants have a high mental health at baseline for both groups >48 (Ware Jr et al., 2000). The QoL was not changed when measuring by Health related quality of life after wearing LWI for 12-months compared with baseline and comparator group (0.7 out 1) (Bennell et al., 2011b). They used a different insole in their study and the period between the two-assessment points was large therefore, no change was shown. In a previous study was performed by Corrêa Dias et al., (2003), the PCS significantly improved after a

combined treatment (exercise and education programme) in individuals with knee OA where there was a significant improvement in knee pain.

4.11.9. Kinematics and kinetics

The ankle ROM in sagittal plane increased significantly after wearing LWI insole for one week compared to baseline. The knee ROM in sagittal plane and ankle dorsiflexion increased significantly after wearing LWI for six weeks compared to baseline. Whereas, the hip and the other knee and ankle angles variables did not change significantly in either LWI or comparator groups compared to baselines or other group. The results of the current study are in agreement with previous study (Jones et al., 2013a). Jones et al., (2013a) found that the maximum knee flexion did not change significantly after wearing LWI for two weeks compared to baseline (standardised shoe). An increasing walking speed in both weeks in both groups compared to baselines. This improvement in walking speed was associated with EKAM reduction in LWI group whereas, the EKAM increased by 0.9% after wearing neutral insole for six weeks in the current study. This increasing in the EKAM, even it was small, may lead to increase disease progression 6.46 times (Miyazaki et al., 2002). In addition, the degree of sagittal ROM of knee and ankle increased with faster acceleration and individuals walked faster after wearing LWI. The improvement in the ROM may explained by a compensatory strategy attempted by the individuals to absorb the extra shock result of faster acceleration (Winter, 1991) or may because of reduction in knee pain. Even the walking speed increased significantly when wearing neutral insole for one and six weeks the GRF increased but not significantly compared to baseline.

Importantly, the knee flexion moment (KFM) increased significantly after wearing LWI for six weeks compared to baseline while there was no changes between groups or week one. The current study found that there was a significant increase in the KFM with a significant reduction in EKAM after wearing LWI for six weeks compared to baseline. However, Walter et al (2010) concluded that increase of the KFM may reduce the effect of the EKAM on the medial contact force and the reduction of the EKAM did not necessary guarantee a reduction in medial contact force due to increase the KFM. However, there was only one participants with neutral knee alignment, and therefore their results can be generalised (Walter et al., 2010). The increasing in the KFM in the current is may be explained as compensatory mechanism to the reduction of the EKAM (Chang et al., 2015). In addition, a large study that evaluated the EKAM, KFM and knee disease progression in individuals with knee OA over 2 years (Change et al., 2015). They found that there was no

correlation between EKAM and KFM and no evidence of an association between peak KFM and disease progression. Whereas, evidence support that EKAM reduction in an effort to delay medial knee OA disease progression (Miyazaki et al., 2002; Change et al., 2015). In addition, EKAM only can measures knee loading on medial compartment knee joint without any contribution from the KFM (Change et al., 2015). An increasing in the KFM did not find in the current study in week one or as immediately effect of LWI in individuals with medial knee OA. This finding is in agreement with Jones et al., (2014) study who did not find a significant change in the KFM when the EKAM was reduced during gait when using LWI in individuals with medial knee OA.

4.12. Limitation of the study

A limitation of this study is that the investigator was not blinded to the kind of the treatment being used in the gait laboratory tests. However, the participants were blinded to the treatments and told that the both types of orthoses are effect in individuals with knee OA with the investigator giving equally supportive responses to the participants' questions. Kinetic and kinematic data was collected through automated measurement tools, so the possibility of the bias was low in term of assessor. The physical activity (volume), questionnaires and balance data was collected without knowledge of the outcomes of the biomechanical data and the data was analysed at the end of the study.

A sample of individuals in the current study was divided randomly into LWI and comparator groups where parallel study design was used. In the study design, participants are then followed over time and their responses to the intervention are compared between groups. This study design (parallel design) is commonly used by researchers to compare between active treatments vs. placebo with no carry-over effects or learning effect that may be experienced with other designs (i.e. cross-over study). Therefore, crossover design need long period between treatment (washout) to reduce the carry-over. The major important consideration when doing a parallel study is randomization to ensure that the results of the study are accurate and have a lower risk of being biased (Foulkes and Mary, 2008). Even the small sample size is considered as a limitation in the current study as parallel study, but because of time limit, the crossover design was not chosen. As parallel design does not require the same number of participants in each group, commonly uses to compare between two control group and treatment group, there is not carry-over or learning effect as crossover, and it would be performed in short time compare to crossover study. More males were recruited in the current study compare to females. However, both genders were invited to participate in the study according to the inclusion criteria.

The duration of wear of the both insoles was six weeks and it is likely that better results may be attained with longer duration. The investigator measured outcome measurements at week one and week six, and this procedure allowed to compare the results to each other. However, some outcomes (i.e. progression of knee OA) was not measured because of the time limit and also as structural changes are generally longer than six weeks, unless expensive MRI is used. Therefore, assessing the effect of LWI for long-term to measure disease progression is need in the future study.

The physical activity was measured in the current study, whereas no information was collected in term of their occupation. The physical activity in the both groups may be affected by the kind of occupation of the participants. However, there was no significant differences in physical activity between both groups at baseline so we can assume that the groups were matched although this is something which should be recorded in future studies.

4.13. Conclusion

The aims of the current study were to determine whether a lateral wedged insoles improved physical activity and pain and whether these improvements concurrent with reductions of the knee loading and then compared their effect with neutral insoles in individuals with medial knee OA. The literature review identified that whilst previous studies have been undertaken on LWI, conflict findings have been found between biomechanical studies and clinical findings, and no differences between LWI and comparator group was found in term of knee pain. In addition, no study has investigated the effect of LWI on activity level as a primary outcome measurement using activity monitor and investigated with knee loading and knee pain at one study. It was hypothesised that the LWI would have an effect on the knee loading and clinical outcomes measures compared to comparator group.

The results of this thesis found that the lateral wedged insole is an efficient intervention to use in individuals with medial knee OA given the reduced the EKAM and KAAI. These reductions in the EKAM and KAAI by wearing the LWI accompanied by a significant clinical improvement (i.e. knee pain and physical activity). Therefore, LWI had a significant effect on the EKAM and thereby, clinical outcomes improved as the result of EKAM reduction. Participants in the LWI group demonstrated faster walking speeds and for longer time. Whereas, the 5˚ LWI (70 shore A) had a significant effect on the EKAM and thereby, clinical outcomes improved as the result of EKAM reduction.

The level of the activity should be measured as a primary outcome and alongside of the EKAM and pain in the future studies with LWI. Future work should investigate whether a combined LWI with other approaches (i.e. exercise or compression sleeves) would have effect on the EKAM, pain and physical activity in long-term treatment.

Chapter Five

General conclusion and future studies

5.1. General conclusion

This thesis conducted to find out the effectiveness of a lateral wedged insole on knee pain, physical activity and joint loading in individuals with medial knee OA during walking. In addition, this study would help researchers and clinicians to determine whether lateral wedged insoles had clinical and biomechanical benefits and consider as an efficient intervention for patients with medial knee OA. The EKAM reduction has been proven in individuals with medial knee OA by wearing LWI but knee pain does not improve significantly compare to comparator insoles. Therefore, knee loading, level of activity and knee pain were assessed after wearing lateral wedged insoles.

In chapter two, literature which linked to knee OA, pain, activity and EKAM was reviewed and critically appraised. As osteoarthritis is one of the most common chronic musculoskeletal disease, joints affected become painful, especially knee joint. The medial compartment of the knee joint is ten times more frequently affected than the lateral compartment, primary reason is that it is exposed to 2.5 times greater load than the lateral compartment during walking. The external knee adduction moment, which is a surrogate measure of the load on the medial compartment during walking, has been found higher in individuals with medial knee OA compared with healthy individuals. The reduction of the EKAM is associated with delay of the disease progression. Lateral wedged insoles are a common conservative treatment and designed to reduce this EKAM which ultimately would aim to have a clinical and biomechanical effects. Evidence has shown that the LWI decreased the EKAM significantly in individuals with medial knee OA; however, pain and function do not improve significantly. Therefore, there are conflicts between biomechanical studies and clinical findings. The reduction of level of physical activity appears in individuals with knee OA and this reduction is mainly due to knee pain and fear of falling during physical activity. An inactive behaviour is the main characteristic of individuals with knee OA and they stepped less than 6000 steps/day. Individuals with knee OA who stepped < 5000 steps/day developed functional limitations 2 years after baseline, and therefore, taking > 6000 steps/day protects individuals with knee OA from functional limitation. Moreover, increasing the number of steps by 1000 steps/day was associated with a 16 to18% lower risk of developing functional limitation. However, evidence has shown that improving the level of activity by stepping more has several benefits for individuals, the

high (>10,000 steps/day) is not recommended for individuals with knee OA because it was associated with 1.32 times greater risk of cartilage lesion. Therefore, the thesis aimed to answer if pain, level of activity and knee loading were changed after wearing LWI for six weeks.

In chapter three, between-day test-retest reliability study was conducted on ten participants with medial knee OA. This repeatability was performed to investigate the consistency of the instruments in producing the same results at two different time points in a medial knee OA population and therefore, an ensure that the change in outcome measures at the end of the intervention are a result of effect of wearing LWIs and not cause of measurement error or investigator mistakes in measuring these outcomes. Repeatability of walking on EKAM and repeatability of star excursion balance test and step test to measure dynamic balance was investigated in this chapter. The data of kinematic and kinetics parameters showed that high between-day test-retest reliability. The EKAM has been demonstrated to have an excellent between-day test-retest reliability to measure load on medial compartment of the knee joint with small SEM and lower minimal detectable difference.

This is the first study to investigate the reliability of the star excursion balance test and step test to measure dynamic balance in individuals with medial knee OA. The star excursion balance test was shown to be more reliable tool to measure dynamic balance in subjects with medial knee OA with excellent ICCs, small SEMs and a lower minimal detectable difference and can accurately determine any improvement in balance after intervention.

From the previous literature, the EKAM has been found to be higher in individuals with medial knee OA compared with healthy individuals. Higher EKAM associated with risk of presence and progression of medial knee OA. Therefore, reducing the EKAM is suggested to be an attractive option to treat medial knee OA. Lateral wedged insoles which are considered as a conservative intervention are used to reduce the EKAM by shifting the ground reaction force laterally, and thereby decreasing the moment arm which results in a reduced the EKAM on the medial compartment of the knee joint and thereby potentially reduce the progression of knee OA. Whilst LWI reduced the EKAM (Barrios et al., 2013), studies have shown that lateral wedge insoles (when compared with a neutral insole) do not reduce pain level (Pham et al., 2004; Baker et al., 2007; Bennell et al., 2011b; Parkers et al., 2013). However, pain level is of utmost importance, the overall activity level of the individual may have changed which may have resulted in more activity with the individual walking to their pain level. Therefore, physical activity level should be measured with lateral wedged insoles alongside knee pain to enable a complete picture when investigation the effect of LWI. The aim of this study to investigate the effectiveness of LWI on knee pain, physical activity and knee loading

in addition to further understand of the effectiveness of the LWI in treat of medial knee OA. In chapter four, twenty participants with medial knee OA were recruited in the current study who randomly assigned into LWI group and comparator group, 10 subjects for each group. They wore the insoles daily for six weeks and monitor for three separate weeks during the experimental period. Participants were assessed at baseline, week one and week six at the University of Salford. The first peak of the EKAM was reduced after wearing LWI for one and six weeks compared baseline, walking speed and knee pain were improved in both assessment point, the activity of the individuals improved by stepping more, walking for long period and became faster. The mobility of the participants improved which was demonstrated by increased walking speed (assessed at the laboratory). As walking speed increased the GRF was also increased but not significant. In this case, the EKAM should be a corresponding increase. However, due to the function of LWI, the EKAM results showed significantly reduced which resulted from the reduction in moment arm by shifting the GRF line laterally to close to the centre of knee joint. The EKAM and level of activity did not change when wearing neutral insole for one or six weeks compared to baseline; however, knee pain improved in both weeks compared to baseline. There was a significant difference between groups in the first peak of the EKAM, level of activity but not in knee pain.

5.2. Novelty of the thesis

The repeatability of the SEBT and ST in measuring of the dynamic balance in individuals with medial knee OA was found that SEBT is more reliable to measure dynamic balance with small SEM and minimum MDD. Therefore, this is the first study that has investigated the repeatability of the SEBT and ST in measuring of the dynamic balance in individuals with medial knee OA.

This study investigated the effectiveness of a LW on knee pain, level of activity and knee loading in individuals with medial knee OA. The LWI was used the first time in 1987 by Sasaki and Yasuda to treat individuals with medial knee OA, the knee pain with analgesic intake were measured in their study. From that date to the present, many researchers investigated the effectiveness of a LWI on knee loading, knee pain and function separately or together with variation in the results. In the current study, combinations of measurements were undertaken in individuals with medial knee OA with LWI. As no study has been undertaken before to measure physical activity as primary outcome using activity monitor alongside knee loading and knee pain at the one study. Finally, in this study the knee loading was measured at three different time-points; at a specific point under stance phase (EKAM), during all the stance phase (KAAI) and during estimated free-living activity (CKL).

However, measuring the medial tibiofemoral compartment load at a specific point during stance phase by the EKAM is essential as a surrogate measuring and measure the load on medial compartment of knee joint during all the stance phase is sensitive method and associated with the symptoms. It is necessary to measure the cumulative knee loading which is a biomechanical approach that integrate the measures of abnormal loading on the tibiofemoral joint during free live activity in this thesis to assess excessive and repetitive loading. Repetitive and excessive loading together on the knee joint are critical factors in the development and progression of knee OA disease. Therefore, this is the first that investigated the effect of LWI on the CKL during walking in individuals with medial knee OA. The results have shown that there was no significant difference after wearing LWI for one or six weeks compared baseline or comparator group. However, the individuals stepped more in LWI group. In the majority of the studies that investigated the effectiveness of LWI in individuals with medial knee OA, knee loading, pain and function were assessed but no study has investigated the effect of LWI on physical activity. Therefore, this is the first study that investigated the effect of LWI on level of physical activity as a primary outcome using activity monitor alongside knee pain and knee loading in individuals with medial knee OA at one study.

Finally, not only number of steps was highlighted in the current study, spent time in different postures (lying/sitting, standing and stepping) and walking patterns (walking length and cadence) has been highlighted as well. This thesis has demonstrated that when investigating interventions in medial knee OA, not only pain should be measured but also the mechanism of the device and also the physical behaviour of the individual. This allows the complete profile of the individual during the treatment period to be ascertained.

5.3. Future studies

A shown in this thesis even though the ST is commonly used in the researches with knee OA and is reliable to measure dynamic balance in individuals with medial knee OA but unfortunately the between-days repeatability was no significant, whereas the between-days repeatability of SEBT was excellent with a significant relationship between sessions. Therefore, repeating this test of the repeatability of SEBT to measure dynamic balance in a much larger sample with medial knee OA is needed. This would then advance the body of evidence for dynamic balance in medial knee OA and incorporate this challenging activity into research studies.

The results of this thesis give the recommendation to measure physical activity as a primary outcome alongside of knee pain. In this thesis, the study was conducted for only six weeks and is not known what the long-term changes in an individual's activity are. Therefore, a longer period of intervention is needed to determine in a future study whether these changes at six weeks are apparent at periods of greater months and longer. If this is the case, then the role of lateral wedge insoles in the treatment of medial knee osteoarthritis is intuitively linked with changes in the wellbeing of the individual. The study design could be further improved to understand the above changes by using a crossover design which is advantageous in study recruitment and would give the changes between treatments in a controlled manner. However, if such a study was being planned, a suitable wash-out period would need to be implemented.

To date, the progression of knee OA has been measured with the EKAM and KAAI (Thorp et al., 2006; Bennell et al., 2011a) or with physical activity (Dore et al., 2013; Lin et al., 2013). However, the progression of knee OA has not been measured with physical activity in present of intervention (i.e. LWI) in the previous literature. Therefore, a future study is recommended to measure these combined measures (knee loading and physical activity) with disease progression in individuals with medial knee OA. As repetitive loading through physical activity (free-living activities) increases the risk of knee OA (Coggon et al., 2000; Vignon et al., 2006). The CKL is an important measure in future studies to further understand of effect of the LWI, especially on progression of knee OA. Whilst the long-term objective would be stability and homeostasis of cartilage, also the shorter time collection of bone marrow lesions (BMLs) would be an advantageous future study.

The effectiveness of the LWI on physical activity was measured at the current study and it was found that this improved. The effectiveness of other treatment (i.e. strengthen exercises, knee braces) on the physical activity is still questionable and if we take physical therapy as one example, we know that dynamic loading is not decreased but pain and function are. Therefore, if we looked at cumulative loading one would expect that greater loads would be placed on the knee and potentially modify disease progression. Therefore, a potential avenue would be combined treatments to investigate the effect of these approaches of treatment on disease progression, knee pain, physical activity, and knee loading in individuals with medial knee OA is recommended.

In summary, in regards to physical activity measures in medial knee OA, this is seen as the start of a journey and thus the future studies in this area would allow further detail on what the individuals were 'doing' rather than what they can do. This is important for future osteoarthritis research given the current challenges in sedentary lifestyle, obesity and risks of cardiovascular health due to these.

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Appendix 1

University of Salford MANCHESTER

Research, Innovation and Academic Engagement Ethical Approval Panel

College of Health & Social Care
AD 101 Allerton Building
University of Salford
M6 6PU

T +44(0)161 295 7016
r.shuttleworth@salford.ac.uk

www.salford.ac.uk/

19 May 2014

Dear Yasser,

RE: ETHICS APPLICATION HSCR14/07 – Test-retest reproducibility of gait and dynamic balance in subjects with medial knee osteoarthritis (OA)

Based on the information you provided, I am pleased to inform you that application HSCR14/07 has been approved.

If there are any changes to the project and/ or its methodology, please inform the Panel as soon as possible.

Yours sincerely,

Rachel Shuttleworth

Rachel Shuttleworth
College Support Officer (R&I)

Appendix 2

University of Salford MANCHESTER

Research, Innovation and Academic Engagement Ethical Approval Panel

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4 June 2014

Dear Yasser,

RE: ETHICS APPLICATION HSCR14/24 – The effectiveness of a lateral Wedge insole on osteoarthritis pain, activity level and joint loading (WPAL study)

Based on the information you have provided, I am pleased to inform you that application HSCR14/24 has been approved.

If there are any changes to the project and/ or its methodology, please inform the Panel as soon as possible.

Yours sincerely,

Rachel Shuttleworth

Rachel Shuttleworth
College Support Officer (R&I)

Appendix 3

Diary Log

WPAL STUDY

Thank you
For
your participation and your time

Participant`s Name

Participant’s Code:

Date	MON	TUE	WED	THU	FRI	SAT	SUN

We would like to thank you for participating in this study,

In order to get information about your daily activities, your pain symptoms, we would be grateful if you would record daily a few comments about your experiences.

This information we gain will be kept in the strictest confidence and only identified by your coding on the front of this booklet.

If you need any information whilst you at home, or have any further questions, please don't hesitate to contact Yasser Althebaity on 07429433980 any time or Chief Investigator: Prof Richard Jones on 01612952295 (daytime).

Once again many thanks for your participation in this study.

Yasser Althebaity
PhD Student
y.m.althebaity@edu.salford.ac.uk
Tel: 07429433980

Prof Richard Jones
Chief Investigator: Pro Richard Jones BSc (Hons), PgCert, PhD
Senior Lecturer in Clinical Biomechanics / Director of the Salford Gait Laboratory
Research Lead: Knee Biomechanics and Injury
PO42 Brian Blatchford Building, University of Salford, M6 6PU
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Instructions

I. ActivPAL3 monitor :

- The activPAL3 should be worn continously for 7 days or until your next visite at University of Salford.
- The activPAL3 should be worn through the day except when swimming/shower.
- Attach the activPAL3 monitor to you middle thigh, above you knee (curved end of monitor towards the hip).
- If you need to remove the monitor and re-placed it again or it starts to become loose, please re-attached with a new stricker.

II. Insole :

- Before your place your insoles in your shoes, first remove any existing insoles. This includes any arched supports that come with the shoe.
- Wear the insoles as much as possible in the same shoe, if so not, please remember to transfer the insole and remove any existing ones from the new pair of shoes.
- The insoles can be worn when you are outside or inside, active or non-active.
- Wear your insoles for as long as possible each day.
- Types of shoe can you wear with inoles :
    - ✓ Lace up
    - ✓ Shoes with strap support
    - ✓ Flat shoes

    X Shoes with medium or high heal
    X Flip flops
    X Shoes which have non removable arched support

- **For the next visits, please wear the same shoes as you used at the first visit**

Please complete all of these questions

Day :

1. How many hours did you use the ActivPal today?

   A. 0 - 6 (___hours) B. 6 - 12 (___hours) C. 12 - 24 (___hours)

2. Have you done any unusual activity today ? Please state (kind/ duration).

……..….
……
……

3. Did you remove it today ?

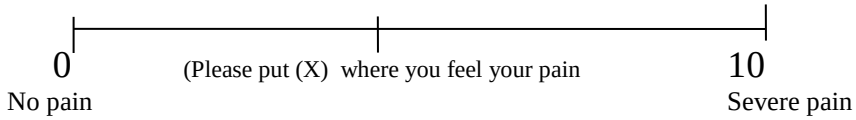
   Yes No

4. If yes, please, state the reason (s) and for how many hours ?

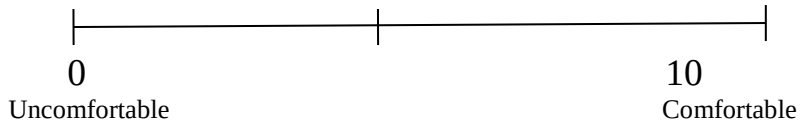
.....

.....

5. How do you feel your pain is today ? (0= no pain, 10= severe pain)



6. How comfortable is the insole today?
   (0=completely uncomfortable 10=completely comfortable)



7. How many hours did you use the insole for today?

   ……..Hours

8. Have you taken any medication for your knee today?

Yes No

Appendix 4

Dear Participant;

Thank you for participation in our study and we would like to inform you that the next week will be the last week to collect your data with insole and monitor device. Therefore, you will find enclosed the monitor device to be placed on your thigh by following the next steps:

1. Stick down the attached adhesive pad (which has two adhesive sides) on the device.
2. Then, place and stick down the device on the middle of your anterior thigh just above your knee joint using the other adhesive side.
3. Please use the waterproof sticker provided to attach the monitor to your thigh.
4. The orientation and position of the device on your thigh must be accurate (please see the picture that the image of the person is upright).
5. The green light (flashing) must appear **at 00:00pm on Monday 00 Jan 2014** (If does not flashing, please text Mr. Yasser ***immediately***, 07429433980).

   N.B. the device has been programmed to start at that time.
6. Please keep wearing insole with the device until your next visit at the University of Salford and wear the same shoes.

   N.B.the next visit will be on **Thu 00 Jan 2014 (0:00-00:00 am)**

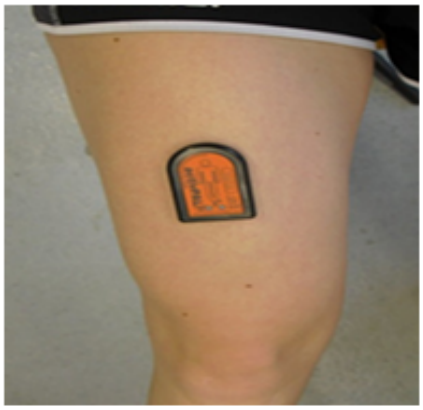


Figure: Location of the monitor

Sincerely,

Chief Investigator

Professor Richard Jones

Principal Investigator

Yasser Althebaity

Appendix 5

Pilot Testing of the protocol

One volunteer with mild medial knee OA was recruited to test the study protocol (male, right knee, age 53, height 171cm, weight 80kg, body mass index 27.36 kg/m²). The study stages were explained and the signed consent form was completed and wore the LWIs for six weeks. The previous protocol was undertaken with high compliance (mean of wear LWI= 7.5 hours/day, mean of placing of activPAL3>12 hours/day, completion the diary). The activities, EKAM, CKL, KAAI, SEBT, ALF, KOOS, and ICOAP are presented in Tables 4-1 and 4-2. The EKAM reduced by using LWI from 0.49 in baseline to 0.45 and 0.38 in week one and week six, respectively. The same effectiveness was found on KAAI which decreased from 0.149 to 0.132 and 0.103 in week one and six, respectively, using LWIs. These reductions associated with decreased knee pain scores, was higher in week six by 16 points in both scores. However, SEBT improved by using LWI by 6.7cm and 5.3cm in anterior and medial directions, respectively, physical function did not change significantly.

However, stepping time decreased in week one compared to the baseline by 18.8 minutes, overall upright time increased in the same week (week one). Because the participant spent more time in standing position (268.97 min) with wearing LWI. standing time, stepping time, and upright time improved to 363.94, 115.10, and 479.04 minutes, respectively, in week six; however, sedentary time declined to 1094.27 and 961.01 minutes in week one and six, respectively. Nevertheless, the number of steps increased in week six to 11833.43 steps/day with LWIs, no improvement in steps has found in week one (decreased to 7260.57 steps/day). Normalised and non-normalised CKL in walking were decreased to 0.48 KNm/kg*s and 38.19 KNms in week one and to 0.61 KNm/kg*s and 48.06 KNms in week six, respectively. Compare to the baseline, the normalised and non-normalised CKL in standing were decreased to 0.33 KNm/kg and 26.32 KNms in week one while in week six they increased to 1.53 KNm/kg and 120.75 KNms, respectively.

The results show that the activity, pain, dynamic balance, and knee loading during walking improved in three sessions (Tables 1 and 2). Cumulative loading in standing increased in week six compared to the baseline. This may have occurred result in pain reduction thereby participant transferred extra load on the right knee and change his standing style by depending on the right knee more (in week six compared to the baseline). We assume that the pain reduction has been found because the participant complained from a little pain at baseline. Even the number of steps decreased in week one, the spent time in standing and totally upright increased. This reduction in number of steps may

be explained by the external factors may be played a role in this reduction for example the bad weather.

When this study was completed, some points have been changed/added;

- Diary, regards (Q1) participants have been asked to be more specific regarding the time (Q1)
  How many hours did you use the activPAL today?
  Before: A. 0-6 B. 6-12 C. 12-14
  New: A. 0-6 (…..hours) B. 6-12 (…..hours) C. 12-14 (…..hours)

- *Diary*, they found it took a long period of time to complete it from the end of week 1 to the begging of week 6 (time consuming).
  Therefore, the log book has been given to the participants in baseline, week 1, and week 5 (with monitor only).

- ActivPAL3 monitor, regards week 5
  Before: sent the device only
  New: the device with instruction sheet will be sent to make sure the device will be fixed in right position and orientation (home visit was recommended as well)

In conclusion, this study was undertaken to test the protocol only. So, it will be difficult to depend on the current result to reflect the effectiveness of LWI on pain, knee loading, and activity.

Table 1: mean of the variables in three sessions

Variable	Baseline	Week_1	Week_6
ALF (sec)	21	===	23
ICOAP	20.4	===	4.5
KOOS pain subscale	67	78	83
SEBT (cm)	A=62.6;M=62.3	=======	A=69.3;M=67.66
Sedentary time (min)/day	1108.71	1094.27	961.01
upright time (min)/day	331.34	345.74	479.04
Stepping time (min)/day	95.57	76.77	115.10
Standing time (min)/day	235.77	268.97	363.94
Standing time (s)/day	14146.29	16138.29	21836.57
Steps/day	9051.71	7260.57	11833.43
EKAM (Nm/kg), walking	0.49	0.45	0.36
EKAM (Nm/kg), standing	0.055	0.02	0,07
CKL (KNm/kg*s), walking	0.67	0.48	0.61
CKL (KNm/kg*s), standing	0.77	0.33	1.53
CKL (KNms),walking	53.88	38.19	48.06
CKL (KNms),standing	61.84	26.32	120.75

Table 2: Mean of the activities variables

	Standing (min)	Stepping (min)	Upright (min)	Sedentary (min)	No steps (steps/day)
Baseline	235.77	95.57	331.34	1108.71	9051.71
Week (1)	268.97	76.77	345.74	1094.27	7260.57
Week (6)	363.94	115.10	479.04	961.01	11833.43